

INVENTOR SEARCH

=> d his 1101

(FILE 'HCAPLUS' ENTERED AT 11:20:11 ON 27 JUL 2007)

L101 26 S L100 AND L50

=> d que 1101

L48 QUE ABB=ON PLU=ON PY<2003 OR PRY<2003 OR AY<2003 OR
MY<2003 OR REVIEW/DT
L50 QUE ABB=ON PLU=ON IMMUNOSUPPRES? OR IMMUNOREG? OR IM
MUN?(A)(SUPPRESS? OR REG?)
L97 1272 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DOHERTY, GEORGE
A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
"MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
"ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98 QUE ABB=ON PLU=ON MERCK?/PA,CS,SO,CO
L99 714 SEA FILE=HCAPLUS ABB=ON PLU=ON L97 AND L48
L100 228 SEA FILE=HCAPLUS ABB=ON PLU=ON L99 AND L98
L101 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L100 AND L50

=> d his 1131

(FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 12:40:59 ON 27
JUL 2007)

L131 6 S L130 AND (L50 OR L59)
SAV L131 JEA176MULTIN/A

FILE 'STNGUIDE' ENTERED AT 12:44:10 ON 27 JUL 2007

FILE 'HCAPLUS' ENTERED AT 12:45:23 ON 27 JUL 2007
SAV L101 JEA176HCPIN/A

FILE 'STNGUIDE' ENTERED AT 12:46:17 ON 27 JUL 2007

=> d que 1131

L48 QUE ABB=ON PLU=ON PY<2003 OR PRY<2003 OR AY<2003 OR
MY<2003 OR REVIEW/DT
L50 QUE ABB=ON PLU=ON IMMUNOSUPPRES? OR IMMUNOREG? OR IM
MUN?(A)(SUPPRESS? OR REG?)
L59 QUE ABB=ON PLU=ON EDG1(A)S1P?
L97 1272 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DOHERTY, GEORGE
A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
"MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
"ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98 QUE ABB=ON PLU=ON MERCK?/PA,CS,SO,CO
L128 608 SEA L97
L129 277 SEA L128 AND L98
L130 143 SEA L129 AND L48
L131 6 SEA L130 AND (L50 OR L59)

=> dup rem 1101 1131

FILE 'HCAPLUS' ENTERED AT 12:49:36 ON 27 JUL 2007

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FILE 'MEDLINE' ENTERED AT 12:49:36 ON 27 JUL 2007

FILE 'BIOSIS' ENTERED AT 12:49:36 ON 27 JUL 2007

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PROCESSING COMPLETED FOR L101

10/501176

PROCESSING COMPLETED FOR L131

L132 29 DUP REM L101 L131 (3 DUPLICATES REMOVED)
 ANSWERS '1-26' FROM FILE HCAPLUS
 ANSWERS '27-29' FROM FILE BIOSIS

INVENTOR SEARCH RESULTS

=> d 1132 1-29 ibib ed ab

L132 ANSWER 1 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2002:301209 HCAPLUS Full-text

DOCUMENT NUMBER: 137:241872

TITLE: Alteration of lymphocyte trafficking by sphingosine-1-phosphate receptor agonists

AUTHOR(S): Mandala, Suzanne; Hajdu, Richard; Bergstrom, James; Quackenbush, Elizabeth; Xie, Jenny; Milligan, James; Thornton, Rosemary; Shei, Gan-Ju; Card, Deborah; Keohane, Carolann; Rosenbach, Mark; Hale, Jeffrey; Lynch, Christopher L.; Rupprecht, Kathleen; Parsons, William; Rosen, Hugh

CORPORATE SOURCE: Departments of Immunology and Rheumatology, Merck Res. Laboratories, Rahway, NJ, 07065, USA

SOURCE: Science (Washington, DC, United States) (2002), 296(5566), 346-349

CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 23 Apr 2002

AB Blood lymphocyte nos., essential for the development of efficient immune responses, are maintained by recirculation through secondary lymphoid organs. We show that lymphocyte trafficking is altered by the lysophospholipid sphingosine-1-phosphate (S1P) and by a phosphoryl metabolite of the immunosuppressive agent FTY720. Both species were high-affinity agonists of at least four of the five S1P receptors. These agonists produce lymphopenia in blood and thoracic duct lymph by sequestration of lymphocytes in lymph nodes, but not spleen. S1P receptor agonists induced emptying of lymphoid sinuses by retention of lymphocytes on the abluminal side of sinus-lining endothelium and inhibition of egress into lymph. Inhibition of lymphocyte recirculation by activation of S1P receptors may result in therapeutically useful immunosuppression.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2000:618629 HCAPLUS Full-text

DOCUMENT NUMBER: 133:275898

TITLE: Efficacy of the echinocandin caspofungin against disseminated aspergillosis and candidiasis in cyclophosphamide-induced immunosuppressed mice

AUTHOR(S): Abruzzo, George K.; Gill, Charles J.; Flattery, Amy M.; Kong, Li; Leighton, Claire; Smith, Jeffrey G.; Pikounis, V. Bill; Bartizal, Ken; Rosen, Hugh

CORPORATE SOURCE: Infectious Diseases, Merck Research Laboratories, Rahway, NJ, 07065-0900, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(9), 2310-2318

CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 06 Sep 2000

AB The in vivo efficacy of the echinocandin antifungal caspofungin acetate (caspofungin; MK-0991) was evaluated in models of disseminated aspergillosis and candidiasis in mice with cyclophosphamide (CY)-induced immunosuppression. Caspofungin is a 1,3- β -D-glucan synthesis inhibitor efficacious against a number of clin. relevant fungi including

Aspergillus and Candida species. Models of CY-induced transient or chronic leukopenia were used with once daily administration of therapy initiated 24 h after microbial challenge. Caspofungin was effective in treating disseminated aspergillosis in mice that were transiently leukopenic (significant prolongation of survival at doses of ≥ 0.125 mg/kg of body weight and a 50% protective dose [PD50] of 0.245 mg/kg/day at 28 days after challenge) or chronically leukopenic (50 to 100% survival at doses of ≥ 0.5 mg/kg and PD50s ranging from 0.173 to 0.400 mg/kg/day). Caspofungin was effective in the treatment and sterilization of Candida infections in mice with transient leukopenia with a 99% ED based on reduction in log10 CFU of Candida albicans/g of kidneys of 0.119 mg/kg and 80 to 100% of the caspofungin-treated mice having sterile kidneys at caspofungin doses from 0.25 to 2.0 mg/kg. In Candida-infected mice with chronic leukopenia, caspofungin was effective at all dose levels tested (0.25 to 1.0 mg/kg), with the log10 CFU of C. albicans/g of kidneys of caspofungin-treated mice being significantly lower (>99% reduction) than that of sham-treated mice from day 4 to day 28 after challenge. Also, 70 to 100% of the caspofungin-treated, chronic leukopenic mice had sterile kidneys at caspofungin doses of 0.5 to 1.0 mg/kg from day 8 to 28 after challenge. Sterilization of Candida infections by caspofungin in the absence of host leukocytes provides compelling in vivo evidence for fungicidal activity against C. albicans. Further human clin. trials with caspofungin against serious fungal infections are in progress.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:566538 HCAPLUS Full-text
DOCUMENT NUMBER: 141:123484
TITLE: Preparation of 1-(amino)indanes and
(1,2-dihydro-3-amino)-benzofurans,
benzothiophenes and indoles as EDG receptor
agonists
INVENTOR(S): Doherty, George A.; Hale,
Jeffrey J.; Mills, Sander G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058149	A2	20040715	WO 2003-US40129	2003 1216

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WO 2004058149	A3	20040916		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2509218	A1	20040715	CA 2003-2509218	2003 1216

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AU 2003297232	A1	20040722	AU 2003-297232
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2003
1216

EP 1581509 A2 20051005 EP 2003-814075

2003
1216

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ,
EE, HU, SK
JP 2006511579 T 20060406 JP 2004-563642

2003
1216

US 2006161005 A1 20060720 US 2005-536730

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0527

US 7220734 B2 20070522
PRIORITY APPLN. INFO.: US 2002-435381P P

2002
1220

WO 2003-US40129 W

2003
1216

OTHER SOURCE(S): MARPAT 141:123484

ED Entered STN: 15 Jul 2004

AB Compds. of formula I [G = C(R4)2, O, S, SO, SO2; X = Ph, alkyl, etc.; Y = (C(R4))p; Z = alkyl, heterocyclo, etc.; A = CO2H, PO3H2, SO3H, tetrazolyl, etc.; each R1 = H, halo, OH, alkyl, alkoxy; R2 = H, halo, OH, alkyl, alkoxy; R3 = H, alkyl; R2R3 = (substituted) alkylene; R4 = H, alkyl; R5 = halo, alkyl, alkoxy; n = 0-1; p = 1-3] are prepared as EDG receptor agonists. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, II was prepared from azetidine-3-carboxylic acid and the prepared indanone derivative The prepared compds. had > 100-fold selectivity of EDG1 over EDG3.

L132 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:412748 HCAPLUS Full-text

DOCUMENT NUMBER: 140:423677

TITLE: Preparation of 3-(tetrahydropyranylamino)cyclo
pentanecarboxylic acid N-benzylamide
derivatives and related compounds as
modulators of chemokine receptor activity

INVENTOR(S): Butora, Gabor; Mills, Sander G.;
Pasternak, Alexander; Shankaran,
Kothandaraman; Yang, Lihu; Zhou, Changyou;
Goble, Stephen D.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 261 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041161	A2	20040521	WO 2003-US33972	

2003
1024

WO 2004041161 A3 20050324

10/501176

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES,
FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU,
SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
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PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

CA 2502174 A1 20040521 CA 2003-2502174
2003
1024

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AU 2003286701 A1 20040607 AU 2003-286701
2003
1024

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EP 1558243 A2 20050803 EP 2003-777911
2003
1024

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ,
EE, HU, SK
JP 2006514003 T 20060427 JP 2004-550126
2003
1024

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US 2006116421 A1 20060601 US 2005-533326
2005
0502

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PRIORITY APPLN. INFO.: US 2002-422451P P
2002
1030

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WO 2003-US33972 W
2003
1024

OTHER SOURCE(S): MARPAT 140:423677

ED Entered STN: 21 May 2004

AB The title compds. (I) [wherein: X = O, NR20, S, SO, SO2, CR21R22, NSO2R20, NCOR20, NCO2R20, CR21CO2R20, CR21OCOR20, CO, OC(Me)20 (where R20 = H, C1-6 alkyl, benzyl, Ph, C3-6 cycloalkyl, etc.; R21, R22 = H, HO, C1-6 alkyl, C1-6 alkoxy, benzyl, Ph, C3-6 cycloalkyl, etc.); R1 = C1-6 alkyl, C1-6 alkoxy-C0-6 alkyl, C1-6 alkyl-S(O)0-2-C0-6-alkyl, N-(un)substituted C1-6 alkylaminosulfonyl-C0-6alkyl, -(C0-6 alkyl)(C3-7 cycloalkyl)(C0-6 alkyl), HO, CO2R20, heterocyclyl, cyano, NR20R26, NR26SO2R20, NR26COR21, OCOR20, Ph (where R26 = H, C1-6 alkyl, benzyl, Ph, etc.); R2, R4, R6 = H, C1-6 alkyl, CF3, CF3O, Cl, Br, Ph; R3 = H, HO, halo, C1-6 alkyl, C1-6 alkoxy, , NR20R21, NR20CO2R21, NR20CONR20OR21, NR20SO2NR20R21, NR20SO2R21, heterocyclyl, cyano, CONR20R21, CO2R20, NO2, SR20, SOR20, SO2R20, SO2NR20R21: R5 = C1-6 alkyl substituted with 1-6 F and optionally substituted with HO, C1-6 alkoxy or CO-C1-6 alkyl each substituted with 1-6 fluoro, C1-6 alkylthio, pyridyl, F, Cl, Br, Ph; R7 = H, C1-6 alkyl, CF3; R8, R9, R10 = H, (un)substituted C1-6 alkyl; or R7 and R8 or R8 and R9 may be joined together to form a ring; R11 = H, C1-6 alkyl, CF3; R27, R28 = oxo, H, Ph, (un)substituted C1-6 alkyl; R29, R30, R31 = H, Me, HO, CF3, MeO, CF3O; or R29 and R9 are connected by a C1-3alkyl bridge; m, n = 0-2; the dashed line = a single or a double bond] and pharmaceutically acceptable salts thereof and individual diastereomers thereof are prepared These compds. are useful as modulators of the chemokine receptor CCR-2 for (a) treating, ameliorating or controlling or reducing the risk of an inflammatory or immunoregulatory disorder or disease or (b) treating, ameliorating or controlling rheumatoid arthritis (no data). Thus, reductive amination of N-[3,5-bis(trifluoromethyl)benzyl]-3-oxo-1-isopropylcyclopentane-1- carboxamide with 4-

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aminotetrahydro-4H-pyran hydrochloride using triacetoxyborohydride in the presence of diisopropylethylamine in CH₂Cl₂ at room temperature overnight gave 46% N-[3,5-bis(trifluoromethyl)benzyl]-3-(tetrahydro-4H-pyran-4-ylamino)-oxo- 1-isopropylcyclopentane-1-carboxamide (II).

L132 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:719274 HCAPLUS Full-text
 DOCUMENT NUMBER: 139:246116
 TITLE: Preparation of aminoalkylphosphonates and related compounds as EDG receptor agonists
 INVENTOR(S): Doherty, George A.; Hale, Jeffrey J.
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 75 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074008	A2	20030912	WO 2003-US7262	2003 0225
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WO 2003074008	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2477449	A1	20030912	CA 2003-2477449	2003 0225
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AU 2003218056	A1	20030916	AU 2003-218056	2003 0225
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EP 1482896	A2	20041208	EP 2003-714037	2003 0225
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005107345	A1	20050519	US 2003-505268	2003 0225
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JP 2005531508	T	20051020	JP 2003-572530	2003 0225
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PRIORITY APPLN. INFO.:			US 2002-360605P	P 2002 0301

10/501176

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WO 2003-US7262 W
2003
0225

OTHER SOURCE(S): MARPAT 139:246116

ED Entered STN: 14 Sep 2003

AB The present invention encompasses title compds., A-X[CR1R2]mCHNH2[CR3R4]pC(R9)3 (m = 1-4; p = 9-20; X = bond, O, NH, S(O)k, k = 0-2; A = CO2H, PO3H2, PO2H2, SO3H, five membered nitrogen containing heterocyclcyl, etc.; two R1 or R3 groups on adjacent carbon may be joined together to form a double bond; R2, R3, R4 = H, halo, OH, CO2H, C1-4 alkyl, alkoxy, alkylthio, aryl, etc.; R1-R4 = residing on the same carbon optionally joined together to form a carbonyl group, etc.; R9 = H, halo, OH, C1-4 alkoxy, alkylthio, C3-7 cycloalkyl, etc.); as well as the pharmaceutically acceptable salts and hydrates thereof. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, preparation of (+/-)-2-amino-4-(4-(octylphenyl))butanol, O-phosphate was described in five steps starting from di-Et 2-acetamido-2-(2-(4-octylphenyl)ethyl)propanedioate.

L132 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:719253 HCAPLUS Full-text

DOCUMENT NUMBER: 139:245479

TITLE: Preparation of aminoalkylphosphonates and related compounds as EDG receptor agonists

INVENTOR(S): Budhu, Richard J.; Doherty, George A.

; Hale, Jeffrey J.; Lynch,

Christopher L.; Mills, Sander G.;

Neway, William E., III

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003073986	A2	20030912	WO 2003-US5947	2003 0227

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WO 2003073986 A3 20040527

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2477423 A1 20030912 CA 2003-2477423

2003
0227

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AU 2003217764 A1 20030916 AU 2003-217764

2003
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EP 1482895 A2 20041208 EP 2003-713727

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EE, HU, SK

JP 2005531506 T 20051020 JP 2003-572508

2003

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US 2006089334 A1 20060427 US 2004-505257

2004

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PRIORITY APPLN. INFO.: US 2002-360663P P

2002

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WO 2003-US5947 W

2003

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OTHER SOURCE(S): MARPAT 139:245479

ED Entered STN: 14 Sep 2003

AB AX(CR1R2)mCH(NH2)(CR3R4)nArBC [A = CO2H, P(O)(OH)2, PH(O)(OH),SO3H, P(O)R5OH, 5-membered N heterocycle; X = bond, O, NH, S, S, S(O), SO2; R1-R4 = H, halogen, OH, CO2H, (un)substituted alkyl, alkoxy, alkylthio, aryl; R1R2, R3R4 = O; m = 1-4; n = 0-4; R5 = (un)substituted alkyl, aryl; Ar = Ph, naphthyl; C = (un)substituted alkyl, alkoxy, acyl, hydroxyalkyl, Ph, heterocyclic, bond; when C = bond, B = (un)substituted Ph, alkyl, alkenyl, alkynyl, OH, SH, acyl, CONH2, NH2; when C = Ph, heterocyclic, B = (un)substituted alkyl, alkoxy, acyl, CO, CH(OH), C6H4, heterocyclic; when C = alkyl, alkoxy, acyl, B = (un)substituted C6H4, heterocyclic] were prepared for use as EDG receptor antagonists useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection (no data). Thus, 4-Me(CH2)7C6H4CH2CH2C(NHAc)(CO2Et)2 was hydrolyzed and decarboxylated to 4-Me(CH2)7C6H4CH2CH2CH(NH2)CO2H which was N-benzyloxycarbonylated, reduced to 4-Me(CH2)7C6H4CH2CH2CH(NHCBz)CH2OH, phosphorylated (MeCH)2NP(OCH2Ph)2, and deblocked to give 4-Me(CH2)7C6H4CH2CH2CH(NH2)CH2OP(O)(OH)2.

L132 ANSWER 7 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591193 HCAPLUS Full-text

DOCUMENT NUMBER: 139:149520

TITLE: Preparation of aralkylpyrrolidines and
-azetidines as Edg receptor agonists

INVENTOR(S): Bugianesi, Robert L.; Doherty, George
A.; Gentry, Amy; Hale, Jeffrey J.
; Lynch, Christopher L.; Mills, Sander
G.; Neway, William E., III

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003062252	A1	20030731	WO 2003-US1196	

2003

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,

10/501176

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL,
PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

CA 2472715 A1 20030731 CA 2003-2472715

2003
0115

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EP 1470137 A1 20041027 EP 2003-705779

2003
0115

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ,
EE, HU, SK

JP 2005515259 T 20050526 JP 2003-562129

2003
0115

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US 2005033055 A1 20050210 US 2004-500895

2004
0707

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PRIORITY APPLN. INFO.: US 2002-350000P P

2002
0118

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WO 2003-US1196 W

2003
0115

OTHER SOURCE(S): MARPAT 139:149520

ED Entered STN: 01 Aug 2003

AB Title compds. I [Ar = (un)substituted Ph, naphthyl; A = CO₂H, P(O)(OH)₂, P(O)OH, SO₃H,
1H-tetrazol-5-yl; R₁, R₂ = H, halogen, OH, CO₂H, (un)substituted alkyl; R₃ = H,
(un)substituted alkyl; m, n = 0, 1] were prepared for use as Edg receptor agonists,
useful for treating immune mediated diseases and conditions, such as bone marrow, organ
and tissue transplant rejection (no data). Thus, 3-pyrrolidinol was converted to di-Et
3-hydroxypyrrolidin-3-ylphosphonate and treated with 4-nonylbenzaldehyde, followed by
ester hydrolysis to give 1-(4-nonylbenzyl)-3-hydroxypyrrolidine-3-phosphonic acid.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 8 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591190 HCAPLUS Full-text

DOCUMENT NUMBER: 139:149756

TITLE: Preparation of N-(benzyl)aminoalkylcarboxylate
s, phosphinates, phosphonates and tetrazoles
as EDG receptor agonists

INVENTOR(S): Doherty, George A.; Li, Zhen
; Hale, Jeffrey J.; Mills,
Sander G.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 152 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

 WO 2003062248 A2 20030731 WO 2003-US1059
 2003
 0114

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 WO 2003062248 A3 20060302
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
 CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,
 GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
 MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE,
 SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
 VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL,
 PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 GW, ML, MR, NE, SN, TD, TG
 CA 2472713 A1 20030731 CA 2003-2472713

2003
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 JP 2005527494 T 20050915 JP 2003-562125

2003
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 EP 1575964 A2 20050921 EP 2003-702110

2003
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 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ,
 EE, HU, SK
 US 2005020837 A1 20050127 US 2004-500811

2004
 0707

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 PRIORITY APPLN. INFO.: US 2002-349995P P

2002
 0118

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 WO 2003-US1059 W
 2003
 0114

OTHER SOURCE(S): MARPAT 139:149756

ED Entered STN: 01 Aug 2003

AB The present invention encompasses preparation of compds., A(CR1R2)nNHCHR3Ar{(R4)0-4}BC
 (Ar = Ph, naphthyl, etc.; A = CO2H, 1H-tetrazol-5-yl, PO3H2, PO2H2, SO3H, PO(R5)OH, R5
 = C1-4 alkyl, hydroxyC1-4alkyl, Ph, COC1-3alkoxy, CH(OH)Ph, etc.; n = 2-4; R1, R2 =
 independently selected from H, halo, OH, CO2H, C1-6 alkyl, Ph, etc.; R3 = H, C1-4
 alkyl, etc.; R4 = CO2H, C1-4 alkyl, sulfonylalkyl, alkoxy, alkoxypropyl, aryl,
 aryloxy, etc.; C = C1-8 alkyl, C1-8 alkoxy, heterocyclyl, etc.; B = (un)substituted Ph,
 (un)substituted C5-16 alkyl, (un)substituted C5-16 alkenyl, (un)substituted C5-16
 alkynyl, etc.), as well as the pharmaceutically acceptable salts and hydrates thereof.
 The compds. are useful for treating immune mediated diseases and conditions, such as
 bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods
 of use are included. Thus, reaction of 3-aminopropylphosphonic acid with 4-
 (decyloxy)benzaldehyde in presence of Bu4NOH and sodium cyanoborohydride in MeOH for 1h
 at 50° gave title compound, N-((4-decyloxy)benzyl)-3-aminopropylphosphonic acid.

L132 ANSWER 9 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:590932 HCAPLUS Full-text
 DOCUMENT NUMBER: 139:149413
 TITLE: Selective S1P1/Edg1 receptor agonists

10/501176

INVENTOR(S): Doherty, George A.; Forrest,
Michael J.; Hajdu, Richard;
Hale, Jeffrey J.; Li, Zhen;
Mandala, Suzanne M.; Mills,
Sander G.; Rosen, Hugh;
Scolnick, Edward M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061567	A2	20030731	WO 2003-US1120	2003 0114
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WO 2003061567	A3	20031224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004058894	A1	20040325	US 2003-339380	2003 0109
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CA 2472680	A1	20030731	CA 2003-2472680	2003 0114
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EP 1469863	A2	20041027	EP 2003-731917	2003 0114
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2003216054	B2	20070104	AU 2003-216054	2003 0114
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US 2005070506	A1	20050331	US 2004-501176	2004 0712
<--				
PRIORITY APPLN. INFO.:			US 2002-349991P	P 2002 0118
<--				
			US 2002-362566P	P 2002 0307
<--				
			US 2002-382933P	P 2002

0523

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 WO 2003-US1120 W
 2003
 0114

ED Entered STN: 01 Aug 2003

AB The present invention encompasses a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1P3/Edg3 receptor, said compound administered in an amount effective for treating said immunoregulatory abnormality. Thus, 4-HOC6H4CHO was treated with Me(CH2)7I to give 4-Me(CH2)7OC6H4CHO which was treated with H2N(CH2)3P(O)(OH)2 to give 4-Me(CH2)7OC6H4CH2NH(CH2)3P(O)(OH)2 which had an EC50 for S1P1 agonism of 1.5 nM and for S1P3 agonism of 6.0 nM.

L132 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:171909 HCAPLUS Full-text

DOCUMENT NUMBER: 136:216887

TITLE: Preparation of phosphate derivatives as immunosuppressants

INVENTOR(S): Mandala, Suzanne; Bergstrom, James;
 Rajdu, Richard; Rosen, Hugh;
 Parsons, William H.; Card, Deborah J.;
 Maccoss, Malcolm

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 59 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002018395	A1	20020307	WO 2001-US26789	2001 0828

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
 CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,
 GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
 MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI,
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
 ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
 CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

CA 2421893	A1	20020307	CA 2001-2421893	2001 0828
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AU 2001085331	A5	20020313	AU 2001-85331	2001 0828
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EP 1315735	A1	20030604	EP 2001-964485	2001 0828
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

10/501176

JP 2004507552 T 20040311 JP 2002-523910 2001
0828
US 2002091105 A1 20020711 US 2001-942411 2001
0830
US 6437165 B2 20020820 US 2000-229438P P 2000
0831
WO 2001-US26789 W 2001
0828

OTHER SOURCE(S): MARPAT 136:216887

ED Entered STN: 08 Mar 2002

AB Immunoregulatory compds. [I; wherein: X = O, S, NR1, (CH2)1-2, optionally substituted with 1-4 halo groups (R1 = H, (C1-C4)alkyl, (C1-C4)haloalkyl); R1a = H, OH, (C1-C4)alkyl, (C1-C4)alkyloxy, the alkyl and alkyloxy portions being optionally substituted with 1-3 halo groups; R1b = H, OH, (C1-C4)alkyl, (C1-C4)haloalkyl; R2 = H, (C1-C4)alkyl, (C1-C4)haloalkyl; and R3 = H, OH, halo, (C1-C4)alkyloxy, (C1-C4)haloalkyloxy], as well as the pharmaceutically acceptable salts and hydrates thereof, are disclosed. Thus, a multistep preparation of 3-amino-3-hydroxymethyl-5-(4-octylphenyl)pentylphosphonic acid is described. The compds. are useful as immunosuppressants, particularly in the treatment of bone marrow and organ transplant rejection. Pharmaceutical compns. and methods of use are included.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:12274 HCAPLUS Full-text

DOCUMENT NUMBER: 134:86272

TITLE: Preparation of pyrimidine derivatives as
Src-family protein tyrosine kinase inhibitor
compounds

INVENTOR(S): Hunt, Julianne A.; Mills, Sander G.;
Sinclair, Peter J.; Zaller, Dennis M.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000214	A1	20010104	WO 2000-US17472	2000 0626

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE,
SN, TD, TG

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CA 2376951 A1 20010104 CA 2000-2376951 2000
0626

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US 6316444 B1 20011113 US 2000-603699 2000
0626

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EP 1194152 A1 20020410 EP 2000-944858 2000
0626

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT, IE, SI, LT, LV, FI, RO
JP 2003503354 T 20030128 JP 2001-505923 2000
0626

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PRIORITY APPLN. INFO.: US 1999-141597P P 1999
0630
<--
WO 2000-US17472 W 2000
0626
<--

OTHER SOURCE(S): MARPAT 134:86272

ED Entered STN: 05 Jan 2001

AB What are claimed are pyrimidine compds. (shown as I), or their pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-associated disorders, such as immune diseases, hyperproliferative disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as cancer, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxycarbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxycarbonyl, carbamoyl, amino, acylamino, alkoxycarbonylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a fused 6-membered aromatic ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, C1-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl (Ph or naphthyl unsubstituted or substituted with 1-3 substituents), or R3 and R5 taken together can represent :O. R4 = H, C1-C6-alkyl, C1-C6-alkoxyl, or R4 and X can join together to form a 5- or 6-membered ring with substituted methylene or ethylene. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5 = N, CH. R7 = H, alkyl, alkoxy, amino. X = O, S, SO, SO2, imino. Z = C:O, SO2, substituted P(:O)(OH) or a single bond. 44 Example preps. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:12273 HCAPLUS Full-text

DOCUMENT NUMBER: 134:86271

TITLE: Preparation of pyrimidine derivatives as
Src-family protein tyrosine kinase inhibitor
compounds

INVENTOR(S): Armstrong, Helen M.; Beresis, Richard; Goulet,
Joung L.; Holmes, Mark A.; Hong, Xingfang;
Mills, Sander G.; Parsons, William H.;
Sinclair, Peter J.; Steiner, Mark G.; Wong,
Frederick; Zaller, Dennis M.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 470 pp.

CODEN: PIXXD2

10/501176

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000213	A1	20010104	WO 2000-US17443	2000 0626

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2383546	A1	20010104	CA 2000-2383546	2000 0626
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EP 1206265	A1	20020522	EP 2000-941701	2000 0626
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EP 1206265	B1	20031112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6498165	B1	20021224	US 2000-604305	2000 0626

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JP 2003523942	T	20030812	JP 2001-505922	2000 0626
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AT 253915	T	20031115	AT 2000-941701	2000 0626
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PRIORITY APPLN. INFO.:	US 1999-141639P	P	1999 0630
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WO 2000-US17443	W	2000 0626
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OTHER SOURCE(S): MARPAT 134:86271

ED Entered STN: 05 Jan 2001

AB What are claimed are pyrimidine compds. (shown as I), or their pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-associated disorders, such as immune diseases, hyperproliferative disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as cancer, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxy-carbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxy-carbonyl, carbamoyl, amino, acylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a

fused 6-membered aromatic ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, C1-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl, or R3 and R5 taken together can represent :O; R3 or R5 can represent a 2 or 3 C methylene bridge forming a ring of 5-8 atoms fused to the A ring. R4 = H, C1-C6-alkyl, C1-C6-alkoxyl. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted or unsubstituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5, X6 = independently N, C, optionally substituted CH. A ring = Ph, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, benzothienyl, benzofuranyl, indolyl, imidazolyl, benzimidazolyl, thiadiazolyl. R7, R8, R9, R10 = independently H, halo, OH, SH, CN, NO2, N3, N2+BF4-, alkyl, alkoxy, alkylthio, sulfinyl, sulfonyl, C1-C6-alkyl, C1-C6-perfluoroalkyl, acyl, alkoxy carbonyl, carbamoyl, acyloxy, alkoxy carbonyloxy, carbamoyloxy, amino, acylamino, ureido, sulfamoyl, sulfonylamino, two of R7, R8, R9, and R10 when on adjacent carbons join together to form a methylenedioxy bridge. N = 0-2. More than 500 example preps. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:900457 HCAPLUS Full-text

DOCUMENT NUMBER: 134:56576

TITLE: Preparation of piperidinylmethylcyclopentanes
as modulators of CCR-5 and/or CCR-3 chemokine
receptors

INVENTOR(S): Finke, Paul E.; Hilfiker, Kerry A.; Loebach,
Jennifer L.; Maccoss, Malcolm; Mills,
Sander G.; Shen, Dong-ming; Oates, Bryan

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 266 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000076514	A1	20001221	WO 2000-US15769	2000 0608

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH,
CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC,
LK, LR, LS, LT, LU, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE,
SN, TD, TG

US 6432981	B1	20020813	US 2000-590484	2000 0608
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PRIORITY APPLN. INFO.: US 1999-138761P P 1999
0611

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OTHER SOURCE(S): MARPAT 134:56576

ED Entered STN: 22 Dec 2000

AB Title compds. I [X = alkylcycloalkylalkyl, alkenyl, alkynyl, alkyl-Y-alkyl, where Y =
bond, O, SO2, NR10, NR10SO2, SO2NR10, S, and SO; R10 = H, (un)substituted alkyl,

10/501176

benzyl, alkylcycloalkyl; R1 = CO₂H, NO₂, tetrazolyl, hydroxyisoxazole, etc; R2 = H, OH; R3 = (un)substituted Ph and heterocycle; Z = (CR₄R₅)_n where n = 1-4; R4 and R5 = independently selected from H, OH, F, (un)substituted alkyl, cycloalkyl, alkenyl, alkynyl, Ph, etc., or R4 and R5 may be joined to form a 3-8 membered (un)substituted saturated ring; R7 = H, OH, halo, (un)substituted alkyl; R8 = H, (un)substituted cycloalkyl, Ph, naphthyl, biphenyl, and heterocycle; W = (CH₂)_x and A = (CH₂)_y where x or y is an integer from 0-2 with the provision the sum of x and y = 2] were prepared for treatment of AIDS, inflammatory and immunoregulatory disorders, asthma, allergic rhinitis, dermatitis, conjunctivitis, atherosclerosis or rheumatoid arthritis (no data). Thus, compd II·HCl was prepared in 5 steps from (+)-trans-3-formyl-4-phenylcyclopentan-1-one. In particular, these compds. are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3 (no data) with application to treatment of HIV.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:900456 HCAPLUS Full-text

DOCUMENT NUMBER: 134:56575

TITLE: Preparation of piperidinylmethylcyclopentanes
as modulators of CCR-5 and/or CCR-3 chemokine
receptors

INVENTOR(S): Finke, Paul E.; Loebach, Jennifer L.; Maccoss,
Malcolm; Mills, Sander G.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 130 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076513	A1	20001221	WO 2000-US15765	2000 0608

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH,
CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE,
SN, TD, TG

US 6506777	B1	20030114	US 2000-589972	2000 0608
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PRIORITY APPLN. INFO.: US 1999-138872P P 1999
0611

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OTHER SOURCE(S): MARPAT 134:56575

ED Entered STN: 22 Dec 2000

AB Title compds. I [X = (un)substituted alkyl-Y-alkyl where Y = CO, CO₂, OCO, OCONR₉, NR₉CO₂, NR₉CONR₁₀; R₉ = H, (un)substituted alkyl, cycloalkyl, alkylcycloalkyl, alkenyl, alkynyl, benzyl or phenyl; R₁₀ = H, (un)substituted alkyl, benzyl or phenyl; R₉ and R₁₀ may be joined together to form a 5-8 membered (un)substituted ring; R1 = CO₂H, NO₂, tetrazolyl, etc.; R2 = H, OH; R3 = (un)substituted Ph and heterocycle; Z = (CR₄R₅)_n where n = 1-4; R4 and R5 = independently H, OH, F, (un)substituted alkyl, cycloalkyl, alkenyl, heterocycle, etc.; R4 and R5 may be joined together to form a 3-8 membered

10/501176

(un)substituted saturated ring; R7 = H, OH, halo, (un)substituted alkyl; R8 = H, (un)substituted Ph, naphthyl, biphenyl, and heterocycle; W = (CH2)x and A = (CH2)y where x or y is an integer from 0-2 with the provision the sum of x and y = 2] were prepared for treatment of AIDS, inflammatory and immunoregulatory disorders, asthma, allergic rhinitis, dermatitis, conjunctivitis, atherosclerosis or rheumatoid arthritis (no data). Thus, compd II·HCl was prepared in 8 steps from Et trans-3-hydroxymethyl-4-phenylcyclopentylacetate. In particular, these compds. are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3 (no data) with application to treatment of HIV.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:900455 HCAPLUS Full-text

DOCUMENT NUMBER: 134:56574

TITLE: Preparation of aminopiperidinylmethylcyclopentanes as modulators of CCR-5 and/or CCR-3 chemokine receptors

INVENTOR(S): Finke, Paul E.; Chapman, Kevin T.; Maccoss, Malcolm; Mills, Sander G.; Oates, Bryan

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 223 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076512	A1	20001221	WO 2000-US15755	2000 0608

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6500844	B1	20021231	US 2000-590487	2000 0608
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PRIORITY APPLN. INFO.: US 1999-139067P P 1999
0611

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OTHER SOURCE(S): MARPAT 134:56574

ED Entered STN: 22 Dec 2000

AB Title compds. I [X = CONR9, NR9CO, OCONR9, NR9CO2, and NR9CONR10; R9 = H, alkyl, cycloalkyl, alkylcycloalkyl, benzyl, Ph, etc.; R10 = H, alkyl, benzyl, or (un)substituted phenyl; R9 and R10 may be joined together to form a 5-8 membered (un)substituted ring; Y = bond, CO, CO2, SO2NR9, alkyl, CONR9, C(S)NR9; Z = bond, NR9, O, alkyl; R1 = (un)substituted Ph, naphthyl, alkyl, cycloalkyl, heterocycle other than tetrazolyl, etc. with provision when Z = NR9, then R9 and R1 may be joined together to form a 5-8 membered (un)substituted cycloalkyl or heterocyclic ring; R2 = H, OH, or R2 and Z may be joined together to form a double bond; R3 = (un)substituted Ph or heterocycle; R7 = H, (un)substituted alkyl, OH, halo; R8 = alkyl, cycloalkyl, alkenyl, (un)substituted Ph, naphthyl, or heterocycle, etc.; W = (CH2)x and A = (CH2)y with

10/501176

proviso that sum of x and y = 2] were prepared for treatment of AIDS, inflammatory and immunoregulatory disorders, asthma, allergic rhinitis, dermatitis, conjunctivitis, atherosclerosis or rheumatoid arthritis (no data). Thus, compound II was prepared in 7 steps from 4-oxo-2-phenylcyclopentanoic acid. In particular, these compds. are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3 (no data) with application to treatment of HIV.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:900454 HCAPLUS Full-text
DOCUMENT NUMBER: 134:56573
TITLE: Preparation of piperidinylmethylcyclopentanes
as modulators of CCR-5 and/or CCR-3 chemokine
receptors
INVENTOR(S): Finke, Paul E.; Maccoss, Malcolm; Millis,
Sander G.; Oates, Bryan
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 277 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076511	A1	20001221	WO 2000-US15657	2000 0608

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH,
CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE,
SN, TD, TG

US 6538002	B1	20030325	US 2000-591631	2000 0608
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PRIORITY APPLN. INFO.: US 1999-138763P P
1999
0611

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OTHER SOURCE(S): MARPAT 134:56573

ED Entered STN: 22 Dec 2000

AB Title compds. I [X = (un)substituted alkenyl, alkynyl, alkyl-Q-alkyl, wherein Q = bond, O, SO₂, NR₁₀, NR₁₀SO₂, SO₂NR₁₀, S, SO and R₁₀ = H, alkyl, benzyl, Ph, etc; Y = bond, CO, CO₂, OCO, SO₂, alkyl, COR₉, NR₉CO, CSNR₉, and NR₉CS, wherein R₉ = H, alkyl, cycloalkyl, benzyl, (un)substituted Ph, etc.; Z = bond, NR₉, O, alkyl; R₁ = (un)substituted Ph, naphthyl, heterocycle, alkyl, etc., or when Z = NR₉, then R₉ and R₁ may be joined together to form a (un)substituted 5-8 membered alkyl or heterocyclic ring; R₂ = H, OH, or R₂ and Z may be joined together to form a double bond; R₃ = (un)substituted Ph or heterocycle; R₇ = H, (un)substituted alkyl, OH, halo, Ph or R₇ and R₈ may be linked together through X to form a substituted 5-membered spirocycloalkyl or spiroheterocyclic derivative; R₈ = H, cycloalkyl, Ph, naphthyl, biphenyl and (un)substituted heterocycle; W = (CH₂)_x and A = (CH₂)_y where x or y is an integer from 0-2 with the provision the sum of x and y = 2] were prepared for treatment of AIDS, inflammatory and immunoregulatory disorders, asthma, allergic rhinitis,

10/501176

dermatitis, conjunctivitis, atherosclerosis or rheumatoid arthritis (no data). Thus, compound II was prepared in 7 steps from 4-oxo-2-phenylcyclopentanoic acid. In particular, these compds. are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3 (no data) with application to treatment of HIV.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:725459 HCAPLUS Full-text

DOCUMENT NUMBER: 133:296373

TITLE: Preparation of 3-phenyl-4-(heterocyclylmethyl)pyrrolidine modulators of chemokine receptor activity

INVENTOR(S): Caldwell, Charles; Chapman, Kevin; Hale, Jeffrey; Kim, Dooseop; Lynch, Christopher; Maccoss, Malcolm; Millis, Sander G.; Willoughby, Christopher; Berk, Scott; Kim, Ronald M.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: PCT Int. Appl., 202 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059498	A1	20001012	WO 2000-US9074	2000 0405

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6498161	B1	20021224	US 2000-543019	2000 0404
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PRIORITY APPLN. INFO.: US 1999-128172P P 1999
0406

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OTHER SOURCE(S): MARPAT 133:296373

ED Entered STN: 13 Oct 2000

AB The title compds. (I) [wherein R1 = CO2H, NO2, tetrazolyl, hydroxyisoxazole, SO2NH(alkyl)R9, or PO3H2; R9 = H, (cyclo)alkyl, benzyl, or (un)substituted phenyl; R2 = (un)substituted piperidinyl, tetrahydropyridinyl, piperazinyl, or 1-oxa-8-azaspiro[4.5]decyl; R3 = (un)substituted Ph or heterocyclyl; R4 = H or (un)substituted alkyl, (alkyl)cycloalkyl, alkenyl, alkynyl, Ph, alkylphenyl, naphthyl, biphenyl, heterocyclyl, cyclohexenyl, etc.; R5 and R6 = independently H or (un)substituted alkyl; or R4 and R5 may be joined together to form an (un)substituted C3-8 cycloalkyl ring; n = 1-3] were prepared as modulators of chemokine receptors, especially the chemokine receptors CCR-5 and/or CCR-3. For example, 2-(R)-((3-(R)-formyl)-4-(S)-3-fluorophenylpyrrolidinyl-1-yl)-3-cyclobutanepropionic acid benzyl ester (preparation given) was treated with Pd/C and dissolved in ClCH2CH2Cl. 4-[N-(pyrimid-2-yl)-N-(prop-

10/501176

1- yl)amino]piperidine•HCl (4-step preparation given), NaBH(OAc)3, and TEA were added, followed by di-tert-butylidicarbonate, to give II. I showed binding activity to the CCR-5 or the CCR-3 receptor, generally with IC50 values of < 1 µM. The present invention is directed to compds. which inhibit the entry of human immunodeficiency virus (HIV) into target cells and are of value in the prevention and treatment of HIV infection and the resulting AIDS syndrome (no data). The invention is further directed to compds. which are useful in the prevention or treatment of certain inflammatory and immunoregulatory disorders, including asthma, allergic rhinitis, dermatitis, conjunctivitis, rheumatoid arthritis, and atherosclerosis (no data).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:725458 HCAPLUS Full-text

DOCUMENT NUMBER: 133:296372

TITLE: Preparation of 3-phenyl-4-(heterocyclylmethyl)pyrrolidine modulators of chemokine receptor activity

INVENTOR(S): Berk, Scott; Caldwell, Charles; Chapman, Kevin; Hale, Jeffrey; Lynch, Christopher; Maccoss, Malcolm; Mills, Sander G.; Willoughby, Christopher

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 200 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000059497	A1	20001012	WO 2000-US9059	2000 0405

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6399619	B1	20020604	US 2000-542898	2000 0404
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PRIORITY APPLN. INFO.: US 1999-128174P P 1999
0406

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OTHER SOURCE(S): MARPAT 133:296372

ED Entered STN: 13 Oct 2000

AB The title compds. (I) [wherein R1 = CO2H, NO2, tetrazolyl, hydroxyisoxazole, SO2NH(alkyl)R9, SO2NHCO(alkyl)R9, or PO3H2; R9 = H, (cyclo)alkyl, benzyl, or (un)substituted phenyl; R2 = (un)substituted piperidinyl, tetrahydropyridinyl, or piperazinyl; R3 = (un)substituted Ph or heterocyclyl; R4 = H or (un)substituted alkyl, (alkyl)cycloalkyl, alkenyl, alkynyl, Ph, alkylphenyl, naphthyl, biphenyl, heterocyclyl, cyclohexenyl, etc.; R5 and R6 = independently H or (un)substituted alkyl; or R4 and R5 may be joined together to form an (un)substituted C3-8 cycloalkyl ring; n = 1-3] were

prepared as modulators of chemokine receptors, especially the chemokine receptors CCR-5 and/or CCR-3. For example, EtNH₂ and 1-tert-butoxycarbonyl-4-piperidone were reacted in the presence of DIEA and reduced with NaBH(OAc)₃ to give 4-(N-ethylamino)-1-tert-butoxycarbonylpiperidine (97%). Addition of carbonyldiimidazole and 3,4-difluorobenzylamine to the piperidine followed by deprotection with TFA afforded 4-(N-(N-(3,4-difluorobenzyl)carbamoyl)-N-ethylamino)piperidine•TFA (45%). Coupling the deprotected piperidine with the aldehyde 2-(R)-(3-(R)-formyl-4-(S)-phenylpyrrolidin-1-yl)-2-(cyclohexyl)acetic acid 4-methoxybenzyl ester (preparation given) in the presence of DIEA followed by reduction with NaBH(OAc)₃ gave II. I showed binding activity to the CCR-5 or the CCR-3 receptor, generally with IC₅₀ values of < 1 μM. The present invention is directed to compds. which inhibit the entry of human immunodeficiency virus (HIV) into target cells and are of value in the prevention and treatment of HIV infection and the resulting AIDS syndrome (no data). The invention is further directed to compds. which are useful in the prevention or treatment of certain inflammatory and immunoregulatory disorders, including asthma, allergic rhinitis, dermatitis, conjunctivitis, rheumatoid arthritis, and atherosclerosis (no data).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L132 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:635463 HCAPLUS Full-text

DOCUMENT NUMBER: 131:243191

TITLE: Spiro-substituted azacycles as modulators of chemokine receptor activity

INVENTOR(S): Mills, Sander G.; MacCoss, Malcolm; Springer, Martin S.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: U.S., 97 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5962462	A	19991005	US 1997-989947	1997 1212
			<--	
PRIORITY APPLN. INFO.:			US 1996-32735P	P 1996 1213
			<--	
			US 1996-33558P	P 1996 1220
			<--	

OTHER SOURCE(S): MARPAT 131:243191

ED Entered STN: 07 Oct 1999

AB The invention is directed to spiro-substituted azacycles which are useful as modulators of chemokine receptor activity. Specifically, I [R₁ = H, (un)substituted alk(en/yn)yl; W = bond, (un)substituted alkylene; Q = (un)substituted NH, O, S, S(O), SO₂; X = bond, (un)substituted alkylene, S, S(O), NHCO, OC(O), etc.; YZ = fused aryl or heteroaryl nucleus; m, n = 0 to 5; (m+n) = 1 to 5] were prepared. The compds. are useful as modulators of the chemokine receptors CCR-1, CCR-2, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CXCR-3, and/or CXCR-4 (no data), and are thereby useful as antiinflammatory and immunomodulating agents. Use for the treatment of HIV infection and/or AIDS is claimed specifically. For instance, 1'-methylspiro[indoline-3,4'-piperidine] underwent a sequence of N-benzoyloxycarbonylation (71%), N'-demethylation (73%), reductive N'-alkylation with a corresponding polyfunctional aldehyde, and removal of the benzoyloxycarbonyl protecting group, to give title compound II.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE

10/501176

IN THE RE FORMAT

L132 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:574297 HCAPLUS Full-text
DOCUMENT NUMBER: 115:174297
TITLE: FK-506 and cyclosporin A: selective inhibition of calcium ionophore-induced polymorphonuclear leukocyte degranulation
AUTHOR(S): Forrest, Michael J.; Jewell, Marvin E.; Koo, Gloria C.; Sigal, Nolan H.
CORPORATE SOURCE: Dep. Immunol. Res., Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Biochemical Pharmacology (1991), 42(6), 1221-8
CODEN: BCPA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 Nov 1991

AB This paper investigates the abilities of FK-506 and cyclosporin A (CsA) to inhibit human polymorphonuclear leukocyte (PMNL) degranulation. PMNLs, purified from human blood, were stimulated in vitro with A23187, ionomycin, the complement derived peptide C5a, formyl-methionylleucinyphenylalanine (FMLP) or phorbol myristate acetate (PMA). Degranulation was assessed by measuring the release of either lactoferrin or N-acetyl- β -D-glucosaminidase (NAG). Both FK-506 and CsA produced a concentration-related inhibition of degranulation induced by either A23187 or ionomycin but did not affect C5a-, FMLP- or PMA-induced degranulation. The IC₅₀ values for inhibition of degranulation (approx. 0.7 nM for FK-506 and 33.7 nM for CsA) are very close to the published values for inhibition of human T-cell proliferation. Removal of calcium from the incubation medium with EGTA totally inhibited calcium ionophore-induced degranulation but had no effect against C5a-, FMLP- or PMA-induced degranulation. Preincubation of PMNLs with actinomycin D or cycloheximide did not affect either A23187- or PMA-induced degranulation. Non-immunosuppressive analogs of CsA were ineffective at inhibiting degranulation. Rapamycin, a macrolide structurally related to FK-506, did not inhibit degranulation but it did antagonize the inhibition produced by FK-506. Given the similar profiles of activity of FK-506 and CsA in neutrophils and T cells, the authors conclude that similar activation or signal transduction pathways may be present in both T cells and neutrophils. Because A23187-induced PMNL degranulation was not sensitive to either actinomycin D or cycloheximide, it is apparent that the signal transduction pathways ultimately control different cellular functions.

L132 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:61838 HCAPLUS Full-text
DOCUMENT NUMBER: 114:61838
TITLE: Process for synthesis of FK-506 C10-C18 intermediates
INVENTOR(S): Jones, Todd K.; Mills, Sander G.; Desmond, Richard
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 4940797	A	19900710	US 1989-327848	1989 0323
			<--	
EP 389244	A1	19900926	EP 1990-302981	1990

10/501176

OTHER SOURCE(S): MARPAT 114:164203

ED Entered STN: 03 May 1991

AB Title compds. I (P, P1 = hydroxy protectant; R1, R2 = H, (substituted C1-4 alkyl, -PhCH2, Ph, with proviso that R2 ≠ H) optically pure are prepared as intermediates for the immunosuppressant FK-506 or intermediates thereof. Title compound I (R1 = Ph; R2 = Me; P1 = 4-(MeO)C6H4CH2; P = PhCH2) was prepared from oxazolidone II.

L132 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:81436 HCAPLUS Full-text

DOCUMENT NUMBER: 114:81436

TITLE: Process for synthesis of FK-506 and tricarboxyl intermediates

INVENTOR(S): Jones, Todd K.; Askin, David; Mills, Sander G.; Reamer, Robert A.; Desmond, Richard; Volante, Ralph P.; Tschaen, David M.; Shinkai, Ichiro

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: Eur. Pat. Appl., 78 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
EP 378318	A1	19900718	EP 1990-300143	1990 0105
			<--	
R: CH, DE, FR, GB, IT, LI, NL CA 2007490	A1	19900711	CA 1990-2007490	1990 0110
			<--	
JP 02233643	A	19900917	JP 1990-4401	1990 0111
			<--	
US 5446158	A	19950829	US 1990-596847	1990 1012
			<--	
PRIORITY APPLN. INFO.:			US 1989-295877	A 1989 0111
			<--	
			US 1989-375091	A 1989 0630
			<--	

OTHER SOURCE(S): MARPAT 114:81436

ED Entered STN: 09 Mar 1991

AB Claimed is a process for synthesizing tricarboxyl compds. RCOCOCOX (I) [R = (substituted) C1-40 alkyl; X = NR1R2, OR1, etc.; R1, R2 = C1-4 alkyl, benzyl, Ph, which may be substituted with halo, C1-4 alkoxy]. The said process comprises the steps of: a) contacting aldehyde RCHO with hydroxyl-protected acetate enolate equivalent Z1OCH:C(OM)X [Z1 = C1-10 alkyl, C6-10 aryl, benzyl (which can be substituted by halo or C1-4 alkoxy), trihydrocarbosilyl; M = Li, Na, K, etc.]; b) deprotecting the 2-hydroxyl function of the resulting product to form RCH(OH)CH(OH)COX (II); c) treating II in an inert, anhydrous, non-hydroxylic solvent with both oxalyl chloride and DMSO under an inert atmospheric at -78° to 0° followed by Et3N for a sufficient time to effect formation of I. Also claimed are intermediates for FK-506, e.g., piperidine III (R =

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H, C1-10 alkyl; Z2 = H, trihydrocarbonyl). The total synthesis of FK-506, a known immunosuppressant, is described.

L132 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:235036 HCAPLUS Full-text

DOCUMENT NUMBER: 112:235036

TITLE: Chemistry of tricarbonyl hemiketals and application of Evans technology to the total synthesis of the immunosuppressant (-)-FK-506

AUTHOR(S): Jones, Todd K.; Reamer, Robert A.; Desmond, Richard; Mills, Sander G.

CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065-0900, USA

SOURCE: Journal of the American Chemical Society (1990), 112(8), 2998-3017
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 112:235036

ED Entered STN: 23 Jun 1990

AB Details of model studies probing the chemical of the tricarbonyl region of FK-506 (I) are presented, and their use in designing a successful route to I is outlined. Applications of asym. oxazolidinone alkylation-aldol methodol. to a convergent, highly flexible synthesis of the C(10)-C(18) fragment and to improvements in the preparation of the C(20)-C(34) segment are also discussed.

L132 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:235199 HCAPLUS Full-text

DOCUMENT NUMBER: 112:235199

TITLE: Process for synthesis of hydroxylactone as intermediate for immunoregulant FK-506

INVENTOR(S): Mills, Sander G.; Volante, Ralph P.; Shinkai, Ichiro

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 343723	A1	19891129	EP 1989-201262	1989 0518
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R: CH, DE, FR, GB, IT, LI, NL US 4940803	A	19900710	US 1988-197551	1988 0523
<--				
JP 02025475	A	19900126	JP 1989-127978	1989 0523
<--				
PRIORITY APPLN. INFO.:			US 1988-197551	A 1988 0523
<--				

OTHER SOURCE(S): CASREACT 112:235199

ED Entered STN: 23 Jun 1990

10/501176

AB Hydroxylactone I (R = H) (II) in optically pure form, useful as an intermediate in the synthesis of the C20-34 chain of the immunosuppressant FK-506 and useful as a precursor for producing an UV radiation absorber, is prepared To a suspension of quinic acid lactone I (R = OH) in ClCH₂CH₂Cl was added thiocarbonyldiimidazole at reflux under N to give 74% thioester III which was refluxed with Bu₃SnH and AIBN in xylene under N to give 43% II.

L132 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1990:234809 HCAPLUS Full-text
 DOCUMENT NUMBER: 112:234809
 TITLE: Process for synthesis of E-2-methyl-
 α,β -unsaturated aldehydes as
 intermediates for the
 immunosuppressant FK-506 and as UV
 absorbers.
 INVENTOR(S): Desmond, Richard; Mills, Sander G.;
 Volante, Ralph P.; Shinkai, Ichiro
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA
 SOURCE: Eur. Pat. Appl., 15 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 343709	A2	19891129	EP 1989-201213	1989 0516
EP 343709	A3	19901205	<--	
R: CH, DE, FR, GB, IT, LI, NL				
US 4914220	A	19900403	US 1989-316607	1989 0227
JP 02025490	A	19900126	JP 1989-127977	1989 0523
JP 06000793	B	19940105	<--	
PRIORITY APPLN. INFO.:			US 1988-197549	A 1988 0523

OTHER SOURCE(S): CASREACT 112:234809; MARPAT 112:234809

ED Entered STN: 23 Jun 1990

AB The title compds. I (Z = triorganosilyl protecting group) are prepared from aldehydes II. I are also useful as UV absorbers (no data). Treatment of imine III with sec-BuLi, followed by reaction with aldehyde IV, treatment of the resulting product with CF₃CO₂H, and hydrolysis, gave 84% (E)-V.

L132 ANSWER 27 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:544668 BIOSIS Full-text
 DOCUMENT NUMBER: PREV200200544668
 TITLE: Phosphate derivatives as immunoregulatory agents.
 AUTHOR(S): Mandala, Suzanne [Inventor, Reprint author];
 Bergstrom, James [Inventor]; Hajdu, Richard
 [Inventor]; Rosen, Hugh [Inventor];
 Parsons, William [Inventor]; Card, Deborah J.

[Inventor]; Maccoss, Malcolm [Inventor]; Kathleen, Rupperecht [Inventor]
CORPORATE SOURCE: Scotch Plains, NJ, USA
ASSIGNEE: Merck and Co., Inc.
PATENT INFORMATION: US 6437165 20020820
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 20, 2002)
Vol. 1261, No. 3. <http://www.uspto.gov/web/menu/patdata.html>. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002
ED Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002
AB Immunoregulatory compounds are disclosed of the formula: ##STR1## as well as the pharmaceutically acceptable salts and hydrates thereof, are disclosed. The compounds are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compositions and methods of use are included.

L132 ANSWER 28 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:505469 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200505469
TITLE: Substituted 3-amino biaryl propionic acids as potent VLA-4 antagonists.
AUTHOR(S): Kopka, Ihor E. [Reprint author]; Lin, Linus S.; Mumford, Richard A.; Lanza, Thomas, Jr.; Magriotis, Plato A.; Young, David; DeLaszlo, Stephen E.; MacCoss, Malcolm; Mills, Sander G.; Van Riper, Gail; McCauley, Ermengilda; Lyons, Kathryn; Vincent, Stella; Egger, Linda A.; Kidambi, Usha; Stearns, Ralph; Colletti, Adria; Teffera, Yohannes; Tong, Sharon; Owens, Karen; Levorse, Dorothy; Schmidt, John A.; Hagmann, William K.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, RY 123-136, PO Box 2000, Rahway, NJ, 07065, USA
ihor_kopka@merck.com
SOURCE: Bioorganic and Medicinal Chemistry Letters, (September, 2002) Vol. 12, No. 17, pp. 2415-2418. print.
CODEN: BMCLE8. ISSN: 0960-894X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002
ED Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002
AB A series of substituted N-(3,5-dichlorobenzenesulfonyl)-(L)-prolyl- and (L)-azetidyl-beta-biaryl beta-alanine derivatives was prepared as selective and potent VLA-4 antagonists. The 2,6-dioxygenated biaryl substitution pattern is important for optimizing potency. Oral bioavailability was variable and may be a result of binding to circulating plasma proteins.

L132 ANSWER 29 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:63645 BIOSIS Full-text
DOCUMENT NUMBER: PREV199598077945
TITLE: The *Saccharomyces cerevisiae* FKS1 (ETG1) gene encodes an integral membrane protein which is a subunit of 1,3-beta-D-glucan synthase.
AUTHOR(S): Douglas, Cameron M.; Foor, Forrest; Marrinan, Jean

10/501176

A.; Morin, Nancy; Nielsen, Jennifer B.; Dahl,
Arlene M.; Mazur, Paul; Baginsky, Walter; Li,
Weili; El-Sherbeini, Mohamed; Clemas, Joseph A.;
Mandala, Suzanne M.; Frommer, Beth R.;
Kurtz, Myra B. [Reprint author]

CORPORATE SOURCE: Merck Res. Lab., PO Box 2000, Rahway, NJ
07065, USA

SOURCE: Proceedings of the National Academy of Sciences of
the United States of America, (1994) Vol.
91, No. 26, pp. 12907-12911.
CODEN: PNASA6. ISSN: 0027-8424.

DOCUMENT TYPE: Article

LANGUAGE: English

OTHER SOURCE: Genbank-U12893

ENTRY DATE: Entered STN: 8 Feb 1995

Last Updated on STN: 14 Mar 1995

ED Entered STN: 8 Feb 1995

Last Updated on STN: 14 Mar 1995

AB In *Saccharomyces cerevisiae*, mutations in FKS1 confer hypersensitivity to the immunosuppressants FK506 and cyclosporin A, while mutations in ETG1 confer resistance to the cell-wall-active echinocandins (inhibitors of 1,3-beta-D-glucan synthase) and, in some cases, concomitant hypersensitivity to the chitin synthase inhibitor nikkomycin Z. The FKS1 and ETG1 genes were cloned by complementation of these phenotypes and were found to be identical. Disruption of the gene results in (i) a pronounced slow-growth phenotype, (ii) hypersensitivity to FK506 and cyclosporin A, (iii) a slight increase in sensitivity to echinocandin, and (iv) a significant reduction in 1,3-beta-D-glucan synthase activity in vitro. The nucleotide sequence encodes a 215-kDa polypeptide predicted to be an integral membrane protein with 16 transmembrane helices, consistent with previous observations that the etg1-1 mutation results in echinocandin-resistant glucan synthase activity associated with the nonextractable membrane fraction of the enzyme. These results suggest that FKS1 encodes a subunit of 1,3-beta-D-glucan synthase. The residual activity present in the disruption mutant, the nonessential nature of the gene, and results of Southern blot hybridization analysis point to the existence of a glucan synthase isozyme.

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=> d his 1133

(FILE 'HCAPLUS, MEDLINE, BIOSIS' ENTERED AT 12:49:36 ON 27 JUL 2007)

L133 4 S (L106 OR L96) AND L101

=> d que 1133

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 106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
 110943-74-3/BI OR 111-70-6/BI OR 111-86-4/BI OR
 1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
 121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
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L3 71 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND 1/NR AND 1/P
 AND 1/N

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L6 23 SEA FILE=REGISTRY ABB=ON PLU=ON L4 AND C4N/RF

L8 36 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND C4S/RF

L9 67 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND C4N/RF

L10 7 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND L9

L11 7 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND C2N2O/RF

L12 1 SEA FILE=REGISTRY ABB=ON PLU=ON L10 AND L11

L13 43 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND 3/F

L14 36 SEA FILE=REGISTRY ABB=ON PLU=ON L13 AND L8

L15 7 SEA FILE=REGISTRY ABB=ON PLU=ON L13 AND L10

L16 12 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND C3N/RF

L17 6 SEA FILE=REGISTRY ABB=ON PLU=ON L16 AND L8

L18 1 SEA FILE=REGISTRY ABB=ON PLU=ON L16 AND L11

L19 40 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND C6/RF AND
 2/NR

L20 9 SEA FILE=REGISTRY ABB=ON PLU=ON L19 AND 4/O

L21 1 SEA FILE=REGISTRY ABB=ON PLU=ON L20 AND C22 H33 N

O4/MF

L22	2	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 1/F
L23	1	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L16 AND 2/NR AND 2/O
L24	22	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 2/NR AND 2-3/O AND C6/RF
L25	11	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L24 AND 2/O
L26	2	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L25 AND 21/C
L27	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L24 AND 20/C AND 3/O
L28	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND 2/BR
L29	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L28 AND 2/NR
L30	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 2/NR AND 5/O AND 1/P
L31	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L15 AND 4/NR
L32	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L31 AND 3/O
L33	27	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L3 AND 4/O
L34	10	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND ?NAPHTH?/CNS
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L41	68	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L3 AND C6/RF
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L46		QUE	ABB=ON	PLU=ON	PHARMAC?/SC, SX
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L50		QUE	ABB=ON	PLU=ON	IMMUNOSUPPRES? OR IMMUNOREG? OR IMMUN?(A) (SUPPRESS? OR REG?)
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L72		QUE	ABB=ON	PLU=ON	INFLAMMATION+PFT, OLD, NT/CT
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L74		QUE	ABB=ON	PLU=ON	INFECTION+PFT, OLD, NT/CT
L75	15	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L74
L76		QUE	ABB=ON	PLU=ON	AIDS+PFT, OLD, NT/CT
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L79	16	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L78
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L86		QUE	ABB=ON	PLU=ON	"SKIN, DISEASE"+PFT, OLD, NT/CT
L87	30	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L86
L88		QUE	ABB=ON	PLU=ON	DERMATITIS+PFT, OLD, NT/CT
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 A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
 AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
 "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
 "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
 L98 QUE ABB=ON PLU=ON MERCK?/PA,CS,SO,CO
 L99 714 SEA FILE=HCAPLUS ABB=ON PLU=ON L97 AND L48
 L100 228 SEA FILE=HCAPLUS ABB=ON PLU=ON L99 AND L98
 L101 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L100 AND L50
 L105 179 SEA FILE=REGISTRY ABB=ON PLU=ON L44 AND 18-70/C
 L106 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L105
 L133 4 SEA (L106 OR L96) AND L101

=> d l133 1-4 ibib ed abs fhitr hitind

L133 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:566538 HCAPLUS Full-text
 DOCUMENT NUMBER: 141:123484
 TITLE: Preparation of 1-(amino)indanes and
 (1,2-dihydro-3-amino)-benzofurans,
 benzothiophenes and indoles as EDG receptor
 agonists
 INVENTOR(S): Doherty, George A.; Hale,
 Jeffrey J.; Mills, Sander G.
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 83 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004058149	A2	20040715	WO 2003-US40129	2003 1216

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WO 2004058149	A3	20040916		
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	CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG,			
	ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,			
	KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,			
	MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO,			
	RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ,			
	UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,			
	AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY,			
	CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,			
	NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,			
	GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2509218	A1	20040715	CA 2003-2509218	2003 1216

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AU 2003297232	A1	20040722	AU 2003-297232	2003 1216
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EP 1581509	A2	20051005	EP 2003-814075	2003 1216
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EE, HU, SK

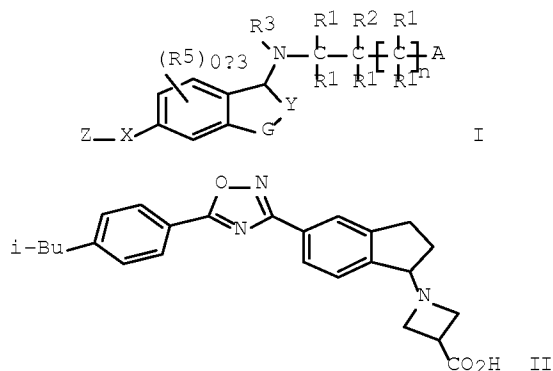
JP 2006511579 T 20060406 JP 2004-563642
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1216

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US 2006161005 A1 20060720 US 2005-536730
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US 7220734 B2 20070522
PRIORITY APPLN. INFO.: US 2002-435381P P
2002
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WO 2003-US40129 W
2003
1216

OTHER SOURCE(S): MARPAT 141:123484
ED Entered STN: 15 Jul 2004
GI



AB Compds. of formula I [G = C(R4)2, O, S, SO, SO2; X = Ph, alkyl, etc.; Y = (C(R4))p; Z = alkyl, heterocyclo, etc.; A = CO2H, PO3H2, SO3H, tetrazolyl, etc.; each R1 = H, halo, OH, alkyl, alkoxy; R2 = H, halo, OH, alkyl, alkoxy; R3 = H, alkyl; R2R3 = (substituted) alkylene; R4 = H, alkyl; R5 = halo, alkyl, alkoxy; n = 0-1; p = 1-3] are prepared as EDG receptor agonists. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compds. and methods of use are included. Thus, II was prepared from azetidine-3-carboxylic acid and the prepared indanone derivative. The prepared compds. had > 100-fold selectivity of EDG1 over EDG3.

IT 350-92-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoindanes as immunosuppressants)
RN 350-92-5 HCAPLUS
CN 2-Propanone, 1,1,1-trifluoro-3-phenyl- (CA INDEX NAME)



IC ICM A61K
 CC 25-23 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
 Section cross-reference(s): 1, 63
 ST aminoindane prepn EDG receptor agonist; indane amino prepn EDG receptor agonist; immunosuppressant aminoindane prepn; benzofuran amino prepn EDG receptor agonist; benzothiophene amino prepn EDG receptor agonist; indole amino prepn EDG receptor agonist
 IT Hepatitis
 (B; preparation of aminoindanes as immunosuppressants)
 IT Inflammation
 (Crohn's disease; preparation of aminoindanes as immunosuppressants)
 IT Intestine, disease
 (Crohn's; preparation of aminoindanes as immunosuppressants)
 IT Kidney, disease
 (Goodpasture's syndrome; preparation of aminoindanes as immunosuppressants)
 IT Eye, disease
 Graves' disease
 (Graves' ophthalmopathy; preparation of aminoindanes as immunosuppressants)
 IT Nervous system, disease
 (Guillain-Barre syndrome; preparation of aminoindanes as immunosuppressants)
 IT Ear, disease
 (Meniere's; preparation of aminoindanes as immunosuppressants)
 IT Skin, neoplasm
 (Sezary syndrome; preparation of aminoindanes as immunosuppressants)
 IT Skin, neoplasm
 (T-cell lymphoma; preparation of aminoindanes as immunosuppressants)
 IT Disease, animal
 (Vogt-Koyanagi-Harada's syndrome; preparation of aminoindanes as immunosuppressants)
 IT Granulomatous disease
 (Wegener's granulomatosis; preparation of aminoindanes as immunosuppressants)
 IT Lung, disease
 (acute injury; preparation of aminoindanes as immunosuppressants)
 IT Injury
 (acute pulmonary; preparation of aminoindanes as immunosuppressants)
 IT Respiratory distress syndrome
 (adult; preparation of aminoindanes as immunosuppressants)
 IT Allergy
 (allergic asthma; preparation of aminoindanes as immunosuppressants)
 IT Allergy
 Eye, disease
 Inflammation
 (allergic conjunctivitis; preparation of aminoindanes as immunosuppressants)
 IT Asthma
 (allergic; preparation of aminoindanes as immunosuppressants)
 IT Jaw
 (alveolar bone; preparation of aminoindanes as immunosuppressants)

IT Edema
(angioneurotic; preparation of aminoindanes as immunosuppressants)

IT Erythropoiesis
(aplasia; preparation of aminoindanes as immunosuppressants)

IT Anemia (disease)
(aplastic; preparation of aminoindanes as immunosuppressants)

IT Alopecia
(areata; preparation of aminoindanes as immunosuppressants)

IT Dermatitis
(atopic; preparation of aminoindanes as immunosuppressants)

IT Anemia (disease)
Autoimmune disease
(autoimmune hemolytic anemia; preparation of aminoindanes as immunosuppressants)

IT Autoimmune disease
Inflammation
Thyroid gland, disease
(autoimmune thyroiditis; preparation of aminoindanes as immunosuppressants)

IT Hepatitis
(autoimmune; preparation of aminoindanes as immunosuppressants)

IT Infection
(bacterial; preparation of aminoindanes as immunosuppressants)

IT Cirrhosis
(biliary; preparation of aminoindanes as immunosuppressants)

IT Bronchi, disease
(bronchiectasis; preparation of aminoindanes as immunosuppressants)

IT Bronchi, disease
Inflammation
(bronchiolitis; preparation of aminoindanes as immunosuppressants)

IT Bronchi, disease
Inflammation
(bronchitis; preparation of aminoindanes as immunosuppressants)

IT Skin, disease
(bullous pemphigoid; preparation of aminoindanes as immunosuppressants)

IT Drug delivery systems
(capsules, soft; preparation of aminoindanes as immunosuppressants)

IT Drug delivery systems
(capsules; preparation of aminoindanes as immunosuppressants)

IT Lung, disease
(chronic obstructive pulmonary disease; preparation of aminoindanes as immunosuppressants)

IT Inflammation
(chronic; preparation of aminoindanes as immunosuppressants)

IT Dermatitis
(contact; preparation of aminoindanes as immunosuppressants)

IT Lymphoma
(cutaneous T-cell; preparation of aminoindanes as immunosuppressants)

IT Kidney, disease
(diabetic nephropathy; preparation of aminoindanes as

immunosuppressants)

IT Connective tissue, disease
Inflammation
(eosinophilic fasciitis; preparation of aminoindanes as immunosuppressants)

IT Granuloma
(eosinophilic; preparation of aminoindanes as immunosuppressants)

IT Skin, disease
(epidermolysis bullosa; preparation of aminoindanes as immunosuppressants)

IT Autoimmune disease
(exptl. autoimmune encephalomyelitis; preparation of aminoindanes as immunosuppressants)

IT Encephalomyelitis
(exptl. autoimmune; preparation of aminoindanes as immunosuppressants)

IT Kidney, disease
(failure; preparation of aminoindanes as immunosuppressants)

IT Lung, disease
(fibrosis; preparation of aminoindanes as immunosuppressants)

IT Ulcer
(gastric; preparation of aminoindanes as immunosuppressants)

IT Digestive tract, disease
Inflammation
(gastroenteritis; preparation of aminoindanes as immunosuppressants)

IT Gingiva, disease
Inflammation
(gingivitis; preparation of aminoindanes as immunosuppressants)

IT Inflammation
Kidney, disease
(glomerulonephritis; preparation of aminoindanes as immunosuppressants)

IT Transplant and Transplantation
(graft-vs.-host reaction; preparation of aminoindanes as immunosuppressants)

IT Kidney, disease
(hemolytic-uremic syndrome; preparation of aminoindanes as immunosuppressants)

IT Infection
(hepatitis B; preparation of aminoindanes as immunosuppressants)

IT Eye, disease
Infection
Inflammation
(herpetic keratitis; preparation of aminoindanes as immunosuppressants)

IT Skin, disease
(hyperproliferation; preparation of aminoindanes as immunosuppressants)

IT Skin, disease
(ichthyosis; preparation of aminoindanes as immunosuppressants)

IT Purpura (disease)
(idiopathic thrombocytopenic; preparation of aminoindanes as immunosuppressants)

IT Intestine, disease
(inflammatory; preparation of aminoindanes as immunosuppressants)

IT Drug delivery systems
(injections; preparation of aminoindanes as immunosuppressants)

IT Reperfusion
(injury; preparation of aminoindanes as immunosuppressants
)

IT Autoimmune disease
(insulin-dependent diabetes mellitus; preparation of aminoindanes as
immunosuppressants)

IT Diabetes mellitus
(insulin-dependent; preparation of aminoindanes as
immunosuppressants)

IT Inflammation
Kidney, disease
(interstitial nephritis; preparation of aminoindanes as
immunosuppressants)

IT Pneumonia
(interstitial; preparation of aminoindanes as
immunosuppressants)

IT Eye, disease
Inflammation
(keratitis; preparation of aminoindanes as
immunosuppressants)

IT Eye, disease
Inflammation
(keratoconjunctivitis; preparation of aminoindanes as
immunosuppressants)

IT Skin, disease
(leukoderma; preparation of aminoindanes as
immunosuppressants)

IT Skin, disease
(lichen planus; preparation of aminoindanes as
immunosuppressants)

IT Necrosis
(liver; preparation of aminoindanes as immunosuppressants)

IT Eye, disease
(macula, senile degeneration; preparation of aminoindanes as
immunosuppressants)

IT Alopecia
(male pattern; preparation of aminoindanes as
immunosuppressants)

IT Anemia (disease)
(megaloblastic anemia; preparation of aminoindanes as
immunosuppressants)

IT Carcinoma
(metastasis; preparation of aminoindanes as
immunosuppressants)

IT Headache
(migraine; preparation of aminoindanes as immunosuppressants
)

IT Erythema
(multiforme; preparation of aminoindanes as
immunosuppressants)

IT Liver, disease
(necrosis; preparation of aminoindanes as immunosuppressants
)

IT Inflammation
Nerve, disease
(neuritis; preparation of aminoindanes as immunosuppressants
)

IT Respiratory distress syndrome
(newborn; preparation of aminoindanes as immunosuppressants
)

IT Hepatitis
(non-A, non-B; preparation of aminoindanes as
immunosuppressants)

IT Diabetes mellitus
(non-insulin-dependent; preparation of aminoindanes as
immunosuppressants)

IT Respiratory system, disease

(obstructive; preparation of aminoindanes as immunosuppressants)

IT Inflammation
Pancreas, disease
(pancreatitis; preparation of aminoindanes as immunosuppressants)

IT Skin, disease
(pemphigus; preparation of aminoindanes as immunosuppressants)

IT Artery, disease
Inflammation
(periarteritis nodosa; preparation of aminoindanes as immunosuppressants)

IT Inflammation
Periodontium, disease
(periodontitis; preparation of aminoindanes as immunosuppressants)

IT Anemia (disease)
(pernicious anemia; preparation of aminoindanes as immunosuppressants)

IT Allergy
(photoallergic contact dermatitis; preparation of aminoindanes as immunosuppressants)

IT Dermatitis
(photoallergic contact; preparation of aminoindanes as immunosuppressants)

IT Myositis
(polymyositis; preparation of aminoindanes as immunosuppressants)

IT Immunosuppressants
(preparation of aminoindanes and amino-benzofurans, benzothiophenes and indoles as immunosuppressants)

IT AIDS (disease)
Acne
Addison's disease
Aging, animal
Agranulocytosis
Allergy
Alopecia
Arteriosclerosis
Asthma
Atherosclerosis
Autoimmune disease
Behcet's syndrome
Burn
Cataract
Celiac disease
Cirrhosis
Cough
Dermatitis
Dermatomyositis
Eczema
Emphysema
Eosinophilia
Erythema
Gingiva, disease
Graves' disease
Hyperthyroidism
Hypoxia
Immune disease
Lung, neoplasm
Lupus erythematosus
Lymph node, disease
Lymphocytic leukemia
Lymphoma
Mastocytoma
Multiple sclerosis

Muscular dystrophy
 Myasthenia gravis
 Myositis
 Necrosis
 Neoplasm
 Obesity
 Osteoporosis
 Periodontium, disease
 Pneumonia
 Psoriasis
 Respiratory system, disease
 Rheumatic fever
 Rheumatoid arthritis
 Sarcoidosis
 Seborrhea
 Sepsis
 Shock (circulatory collapse)
 Sjogren syndrome
 Thrombosis
 Transformation, neoplastic
 Transplant rejection
 Ulcer
 Urticaria
 (preparation of aminoindanes as immunosuppressants)
 IT Biliary tract, disease
 (primary biliary cirrhosis; preparation of aminoindanes as
 immunosuppressants)
 IT Inflammation
 Intestine, disease
 (pseudomembranous enterocolitis; preparation of aminoindanes as
 immunosuppressants)
 IT Fibrosis
 (pulmonary; preparation of aminoindanes as
 immunosuppressants)
 IT Skin, disease
 (pyoderma; preparation of aminoindanes as immunosuppressants
)
 IT Injury
 (reperfusion; preparation of aminoindanes as
 immunosuppressants)
 IT Eye, disease
 Inflammation
 (retinitis pigmentosa; preparation of aminoindanes as
 immunosuppressants)
 IT Inflammation
 Nose, disease
 (rhinitis; preparation of aminoindanes as immunosuppressants
)
 IT Connective tissue, disease
 (scleroderma; preparation of aminoindanes as
 immunosuppressants)
 IT Biliary tract, disease
 Inflammation
 (sclerosing cholangitis; preparation of aminoindanes as
 immunosuppressants)
 IT Mental and behavioral disorders
 (senile psychosis; preparation of aminoindanes as
 immunosuppressants)
 IT Shock (circulatory collapse)
 (septic; preparation of aminoindanes as immunosuppressants
)
 IT Disease, animal
 (siderosis; preparation of aminoindanes as
 immunosuppressants)
 IT Drug delivery systems
 (suspensions; preparation of aminoindanes as
 immunosuppressants)

IT Lupus erythematosus
(systemic; preparation of aminoindanes as immunosuppressants)

IT Drug delivery systems
(tablets; preparation of aminoindanes as immunosuppressants)

IT Injury
(trauma; preparation of aminoindanes as immunosuppressants)

IT Stomach, disease
(ulcer; preparation of aminoindanes as immunosuppressants)

IT Inflammation
Intestine, disease
(ulcerative colitis; preparation of aminoindanes as immunosuppressants)

IT Eye, disease
Inflammation
(uveitis; preparation of aminoindanes as immunosuppressants)

IT Blood vessel, disease
Inflammation
(vasculitis; preparation of aminoindanes as immunosuppressants)

IT Infection
(viral hepatitis; preparation of aminoindanes as immunosuppressants)

IT Hepatitis
(viral; preparation of aminoindanes as immunosuppressants)

IT 721948-69-2P 721948-70-5P 721948-71-6P 721948-72-7P
721948-73-8P 721948-74-9P 721948-75-0P 721948-76-1P
721948-77-2P 721948-78-3P 721948-79-4P 721948-80-7P
721948-81-8P 721948-82-9P 721948-83-0P 721948-84-1P
721948-85-2P 721948-86-3P 721948-87-4P 721948-88-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(preparation of aminoindanes as immunosuppressants)

IT 95-48-7, o-Cresol, reactions 350-92-5 623-51-8, Ethyl
mercaptoacetate 625-36-5, 3-Chloropropionyl chloride 629-27-6,
1-Iodoctane 2550-36-9, Bromomethylcyclohexane 3470-49-3,
5-Hydroxy-1-indanone 20029-52-1, 4-Cyclohexylbenzoic acid
25724-79-2, 5-Cyano-1-indanone 34598-49-7, 5-Bromo-1-indanone
36476-78-5, Azetidine-3-carboxylic acid 38861-88-0,
4-(2-Methylpropyl)benzoic acid 100202-39-9, Methyl
azetidine-3-carboxylate hydrochloride 146631-00-7,
4-Benzylloxyphenylboronic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoindanes as immunosuppressants)

IT 125114-88-7P 146936-34-7P 167279-18-7P
208108-76-3P 256488-46-7P 685529-03-7P
721948-89-6P 721948-90-9P 721948-91-0P 721948-92-1P
721948-93-2P 721948-94-3P 721948-95-4P 721948-96-5P
721948-97-6P 721948-98-7P 721948-99-8P 721949-00-4P
721949-01-5P 721949-02-6P 721949-03-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation of aminoindanes as immunosuppressants)

L133 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:591193 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149520
TITLE: Preparation of aralkylpyrrolidines and
-azetidines as Edg receptor agonists
INVENTOR(S): Bugianesi, Robert L.; Doherty, George
A.; Gentry, Amy; Hale, Jeffrey J.
; Lynch, Christopher L.; Mills, Sander
G.; Neway, William E., III

10/501176

PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 112 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062252	A1	20030731	WO 2003-US1196	2003 0115

<--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2472715	A1	20030731	CA 2003-2472715	2003 0115
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EP 1470137	A1	20041027	EP 2003-705779	2003 0115
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

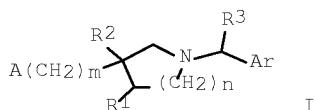
JP 2005515259	T	20050526	JP 2003-562129	2003 0115
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US 2005033055	A1	20050210	US 2004-500895	2004 0707
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PRIORITY APPLN. INFO.:	US 2002-350000P	P	2002 0118
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WO 2003-US1196	W	2003 0115
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OTHER SOURCE(S): MARPAT 139:149520
 ED Entered STN: 01 Aug 2003
 GI

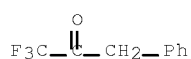


AB Title compds. I [Ar = (un)substituted Ph, naphthyl; A = CO₂H, P(O)(OH)₂, P(O)OH, SO₃H, 1H-tetrazol-5-yl; R₁, R₂ = H, halogen, OH, CO₂H, (un)substituted alkyl; R₃ = H, (un)substituted alkyl; m, n = 0, 1] were prepared for use as Edg receptor agonists, useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection (no data). Thus, 3-pyrrolidinol was converted to di-Et 3-hydroxypyrrolidin-3-ylphosphonate and treated with 4-nonylbenzaldehyde, followed by ester hydrolysis to give 1-(4-nonylbenzyl)-3-hydroxypyrrolidine-3-phosphonic acid.

IT 350-92-5, 1,1,1-Trifluoro-3-phenyl-2-propanone
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

RN 350-92-5 HCAPLUS

CN 2-Propanone, 1,1,1-trifluoro-3-phenyl- (CA INDEX NAME)



IC ICM C07F009-38

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1

ST Edg receptor agonist aralkylpyrrolidine aralkylazetidine prepn immunosuppressant

IT Chronic lymphocytic leukemia
 Human
 Immunosuppressants
 Lymphoma
 Multiple sclerosis
 Psoriasis
 Rheumatoid arthritis
 Transplant rejection
 (preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

IT Lupus erythematosus
 (systemic; preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

IT 96-33-3, Methyl acrylate 100-83-4, 3-Hydroxybenzaldehyde
 107-13-1, Acrylonitrile, reactions 111-70-6, 1-Heptanol
 121-32-4, 3-Ethoxy-4-hydroxybenzaldehyde 121-33-5,
 4-Hydroxy-3-methoxybenzaldehyde 123-08-0, 4-Hydroxybenzaldehyde
 350-92-5, 1,1,1-Trifluoro-3-phenyl-2-propanone 406-94-0,
 trans-4,4-Trifluoro-2-butenic acid 619-66-9, 4-Formylbenzoic
 acid 623-27-8, Terephthalaldehyde 623-51-8, Ethyl
 mercaptoacetate 629-27-6, 1-Iodooctane 682-30-4, Diethyl
 vinylphosphonate 2420-16-8, 3-Chloro-4-hydroxybenzaldehyde
 2495-35-4, Benzyl acrylate 2973-76-4, 3-Bromo-4-hydroxy-5-
 methoxybenzaldehyde 2973-77-5, 3,5-Dibromo-4-
 hydroxybenzaldehyde 6138-90-5, Geranyl bromide 7770-45-8,
 4-Hydroxy-1-naphthaldehyde 15174-69-3, 4-Hydroxy-3-
 methylbenzaldehyde 32247-96-4, 3,5-Bis(trifluoromethyl)benzyl
 bromide 36476-78-5, 3-Azetidinecarboxylic acid
 38841-98-4, Octylmagnesium chloride 40499-83-0,
 3-Hydroxypyrrolidine 54256-43-8, 4-Decylbenzoyl chloride
 54963-70-1, 4-Nonylbenzoyl chloride 56962-11-9,
 2-Chloro-4-hydroxybenzaldehyde 64283-87-0, 4-Phenylbutyl iodide
 65695-05-8 93102-05-7 570424-02-1 570424-08-7
 570424-09-8 570424-10-1 570424-11-2
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of aralkylpyrrolidines and -azetidines as Edg receptor

agonists)

IT 17012-21-4P 24076-33-3P, 3-Methoxy-4-(octyloxy)benzaldehyde 24083-12-3P, 3-Octyloxybenzaldehyde 24083-13-4P, 4-Octyloxybenzaldehyde 54784-14-4P, 4-(Octyloxy)-1-naphthaldehyde 59378-87-9P, 3-Pyrrolidinecarboxylic acid 62299-38-1P 70972-98-4P, 4-Nonylbenzaldehyde 70972-99-5P, 4-Decylbenzaldehyde 101385-93-7P 103057-44-9P 108898-23-3P 131888-48-7P 146936-34-7P 167279-18-7P 188846-99-3P 198959-37-4P 208108-76-3P 246847-91-6P 256488-46-7P 569684-92-0P 569684-93-1P 569684-95-3P 569685-33-2P 569685-34-3P 569685-42-3P 569685-43-4P 569685-49-0P 569685-50-3P 570423-86-8P 570423-87-9P 570423-88-0P 570423-89-1P 570423-90-4P 570423-91-5P 570423-92-6P 570423-93-7P 570423-94-8P 570423-95-9P 570423-96-0P 570423-97-1P 570423-98-2P 570423-99-3P 570424-00-9P 570424-01-0P 570424-03-2P 570424-04-3P 570424-05-4P 570424-06-5P 570424-07-6P 570424-13-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

IT 570423-28-8P 570423-29-9P 570423-30-2P 570423-31-3P 570423-32-4P 570423-33-5P 570423-34-6P 570423-35-7P 570423-36-8P 570423-37-9P 570423-38-0P 570423-39-1P 570423-40-4P 570423-41-5P 570423-42-6P 570423-43-7P 570423-44-8P 570423-45-9P 570423-46-0P 570423-47-1P 570423-48-2P 570423-49-3P 570423-50-6P 570423-51-7P 570423-52-8P 570423-53-9P 570423-54-0P 570423-55-1P 570423-56-2P 570423-57-3P 570423-58-4P 570423-59-5P 570423-61-9P 570423-62-0P 570423-63-1P 570423-64-2P 570423-65-3P 570423-66-4P 570423-67-5P 570423-68-6P 570423-69-7P 570423-70-0P 570423-71-1P 570423-72-2P 570423-73-3P 570423-74-4P 570423-75-5P 570423-76-6P 570423-77-7P 570423-78-8P 570423-79-9P 570423-80-2P 570423-81-3P 570423-82-4P 570423-83-5P 570423-84-6P 570423-85-7P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

IT 570424-12-3

RL: RCT (Reactant); RACT (Reactant or reagent) ('preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591190 HCAPLUS Full-text

DOCUMENT NUMBER: 139:149756

TITLE: Preparation of N-(benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists

INVENTOR(S): Doherty, George A.; Li, Zhen; Hale, Jeffrey J.; Mills, Sander G.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 152 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

10/501176

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062248	A2	20030731	WO 2003-US1059	2003 0114

WO 2003062248 A3 20060302
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2472713	A1	20030731	CA 2003-2472713	2003 0114
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JP 2005527494	T	20050915	JP 2003-562125	2003 0114
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EP 1575964	A2	20050921	EP 2003-702110	2003 0114
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 US 2005020837 A1 20050127 US 2004-500811

PRIORITY APPLN. INFO.:	US 2002-349995P	P	2002 0118
	WO 2003-US1059	W	2003 0114

OTHER SOURCE(S): MARPAT 139:149756

ED Entered STN: 01 Aug 2003

AB The present invention encompasses preparation of compds., A(CR1R2)nnHCHR3Ar{(R4)0-4}BC (Ar = Ph, naphthyl, etc.; A = CO2H, 1H-tetrazol-5-yl, PO3H2, PO2H2, SO3H, PO(R5)OH, R5 = C1-4 alkyl, hydroxyC1-4alkyl, Ph, COC1-3alkoxy, CH(OH)Ph, etc.; n = 2-4; R1, R2 = independently selected from H, halo, OH, CO2H, C1-6 alkyl, Ph, etc.; R3 = H, C1-4 alkyl, etc.; R4 = CO2H, C1-4 alkyl, sulfonylalkyl, alkoxy, alkoxycyclopropyl, aryl, aryloxy, etc.; C = C1-8 alkyl, C1-8 alkoxy, heterocyclyl, etc.; B = (un)substituted Ph, (un)substituted C5-16 alkyl, (un)substituted C5-16 alkenyl, (un)substituted C5-16 alkynyl, etc.), as well as the pharmaceutically acceptable salts and hydrates thereof. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, reaction of 3-aminopropylphosphonic acid with 4-(decyloxy)benzaldehyde in presence of Bu4NOH and sodium cyanoborohydride in MeOH for 1h at 50° gave title compound, N-((4-decyloxy)benzyl)-3-aminopropylphosphonic acid.

IT 569682-66-2P

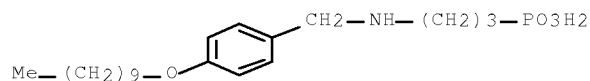
10/501176

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

RN 569682-66-2 HCAPLUS

CN Phosphonic acid, [3-[[[4-(decyloxy)phenyl]methyl]amino]propyl]-(9CI) (CA INDEX NAME)



IC ICM C07F

CC 29-7 (Organometallic and Organometalloidal Compounds)

Section cross-reference(s): 1, 63

IT Inflammation

(Crohn's disease; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Asthma

(Graves ophthalmopathy; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Lymphoma

(acute and chronic; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Arthritis

(chronic rheumatoid; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Inflammation

(chronic; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Skin, disease

(ichthyosis, bullous; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Autoimmune disease

(insulin-dependent diabetes mellitus; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Autoimmune disease

Cardiovascular agents

Cardiovascular system

Chronic lymphocytic leukemia

Cirrhosis

Drug delivery systems

Human

Immunosuppressants

Immunosuppression

Mammalia

Multiple sclerosis

(preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Lupus erythematosus

(systemic; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Inflammation

Intestine, disease

(ulcerative colitis; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT Eye, disease

Inflammation

(uveitis; preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT 569682-66-2P 569682-67-3P 569682-68-4P
 569682-69-5P 569682-70-8P 569682-71-9P
 569682-72-0P 569682-73-1P 569682-74-2P
 569682-75-3P 569682-76-4P 569682-77-5P
 569682-78-6P 569682-79-7P 569682-80-0P 569682-81-1P
 569682-82-2P 569682-83-3P 569682-84-4P 569682-85-5P
 569682-86-6P 569682-87-7P 569682-89-9P
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 569683-51-8P 569683-53-0P 569683-55-2P
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 569684-81-7P 569684-82-8P 569684-83-9P
 569684-84-0P 569684-85-1P 569684-86-2P
 569684-87-3P 569684-88-4P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of (benzyl)aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as EDG receptor agonists)

IT 56-12-2, reactions 64-04-0, Benzeneethanamine 75-07-0, Acetaldehyde, reactions 83-38-5 98-80-6, Phenylboronic acid 100-52-7, Benzaldehyde, reactions 103-63-9, Phenethyl bromide 106-41-2, 4-Bromophenol 107-08-4, 1-Iodopropane 107-13-1, Acrylonitrile, reactions 107-95-9, β -Alanine 111-70-6, 1-Heptanol 111-86-4, Octylamine 112-31-2, n-Decanal

121-32-4, 3-Ethoxy-4-hydroxybenzaldehyde 121-33-5 123-08-0,
 4-Hydroxybenzaldehyde 123-38-6, Propanal, reactions 139-85-5,
 3,4-Dihydroxybenzaldehyde 143-16-8 144-90-1 350-92-5
 437-81-0 541-48-0 542-69-8, 1-Iodobutane 556-18-3,
 4-Aminobenzaldehyde 565-71-9 589-29-7, 1,4-Benzenedimethanol
 591-20-8, 3-Bromophenol 616-76-2 619-66-9,
 4-Carboxybenzaldehyde 623-27-8, 1,4-Benzenedicarboxaldehyde
 623-51-8, Ethyl mercaptoacetate 629-27-6, 1-Iodooctane
 637-59-2 638-45-9, 1-Iodohexane 660-88-8 764-85-2, Nonanoyl
 chloride 924-49-2 2050-77-3, 1-Iododecane 2052-07-5
 2113-57-7 2233-18-3 2314-36-5 2374-05-2,
 4-Bromo-2,6-dimethylphenol 2420-16-8, 3-Chloro-4-
 hydroxybenzaldehyde 2439-54-5 2973-76-4 2973-78-6
 3111-37-3 3132-99-8, 3-Bromobenzaldehyde 3261-62-9
 3300-51-4 3453-33-6, 6-Methoxy-2-naphthaldehyde
 3761-92-0, Hexylmagnesium bromide 3964-56-5 4282-40-0,
 1-Iodoheptane 4282-42-2, 1-Iodononane 4282-44-4,
 1-Iodoundecane 4815-96-7 5438-36-8 5699-54-7 6323-99-5
 7013-05-0 7368-78-7, 4-Bromo-2-methoxyphenol 7463-51-6,
 4-Bromo-3,5-dimethylphenol 7530-27-0 7770-45-8 10521-91-2,
 5-Phenyl-1-pentanol 13138-33-5, 3-Aminopropylphosphonic acid
 13214-66-9, Benzenebutanamine 13477-53-7 13880-74-5
 18278-34-7, 4-Hydroxy-2-methoxybenzaldehyde 19463-48-0
 23703-22-2 25006-17-1 35622-27-6 38841-98-4, Octylmagnesium
 chloride 40371-51-5 49763-66-8, 4-Octylbenzaldehyde
 51554-95-1 56217-93-7, 1H-Tetrazole-5-propanamine 56962-11-9,
 2-Chloro-4-hydroxybenzaldehyde 58521-63-4 64283-87-0
 65564-05-8, 3-(Benzyloxycarbonylamino)propanal 65600-74-0,
 Ethyldiethoxymethyl phosphinate 65695-05-8 70547-87-4
 70972-98-4, 4-Nonylbenzaldehyde 70972-99-5 76287-49-5
 76542-24-0, 1-Bromo-4-(nonylthio)benzene 103680-71-3
 127729-35-5 130592-02-8 148547-19-7, Methyl
 4-bromo-3-methylbenzoate 495397-19-8 569684-89-5 569685-44-5
 569685-48-9 569685-53-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of (benzyl)aminoalkylcarboxylates, phosphinates,
 phosphonates and tetrazoles as EDG receptor agonists)

IT 24076-33-3P 24083-13-4P, 4-Octyloxybenzaldehyde 30609-20-2P
 50262-46-9P 54784-14-4P 56308-79-3P 56741-21-0P
 60951-75-9P 61343-82-6P 71434-34-9P 75472-36-5P
 75677-08-6P 78119-82-1P, 6-Hydroxy-2-naphthaldehyde
 83697-65-8P 93972-07-7P 93972-08-8P 99186-35-3P,
 4-Hydroxy-3-propyloxybenzaldehyde 101500-22-5P 103680-62-2P
 108898-23-3P 121118-78-3P 123912-25-4P 131888-48-7P
 143230-66-4P 149104-89-2P, 4-Bromo-3-methylbenzyl alcohol
 167279-18-7P 169806-13-7P 208108-76-3P
 221018-00-4P, [1,1':2',1''-Terphenyl]-4-carboxaldehyde
 226408-14-6P, [1,1':3',1''-Terphenyl]-4-carboxaldehyde
 246847-91-6P 256488-46-7P 500191-05-9P 569684-90-8P
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 569685-52-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

10/501176

(Preparation); RACT (Reactant or reagent)
(preparation of (benzyl)aminoalkylcarboxylates, phosphinates,
phosphonates and tetrazoles as EDG receptor agonists)

L133 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:590932 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149413
TITLE: Selective 5iPl/Edg1
receptor agonists
INVENTOR(S): Doherty, George A.; Forrest,
Michael J.; Hajdu, Richard;
Hale, Jeffrey J.; Li, Zhen;
Mandala, Suzanne M.; Mills,
Sander G.; Rosen, Hugh;
Scolnick, Edward M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
WO 2003061567	A2	20030731	WO 2003-US1120	2003 0114
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WO 2003061567	A3	20031224		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2003216054	B2	20070104	AU 2003-216054	2003 0114
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US 2005070506	A1	20050331	US 2004-501176	2004 0712
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PRIORITY APPLN. INFO.:			US 2002-349991P	P

2002
0118

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WO 2003-US1120 W
2003
0114

ED Entered STN: 01 Aug 2003

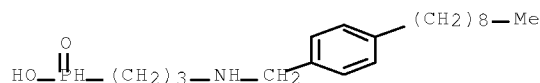
AB The present invention encompasses a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor, said compound administered in an amount effective for treating said immunoregulatory abnormality. Thus, 4-HOC6H4CHO was treated with Me(CH2)7I to give 4-Me(CH2)7OC6H4CHO which was treated with H2N(CH2)3P(O)(OH)2 to give 4-Me(CH2)7OC6H4CH2NH(CH2)3P(O)(OH)2 which had an EC50 for S1P1 agonism of 1.5 nM and for S1P3 agonism of 6.0 nM.

IT 569684-52-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

RN 569684-52-2 HCAPLUS

CN Phosphinic acid, [3-[[[(4-nonylphenyl)methyl]amino]propyl]- (9CI)
(CA INDEX NAME)



IC ICM A61K

CC 29-7 (Organometallic and Organometalloidal Compounds)

Section cross-reference(s): 1, 10, 25, 63

IT Hepatitis

(B, acute; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Inflammation

(Crohn's disease; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Intestine, disease

(Crohn's; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT G protein-coupled receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-1 (endothelial differentiation gene 1); preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT G protein-coupled receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

- (EDG-3 (endothelial differentiation gene 3); preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Anemia (disease)
(Fanconi's; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Kidney, disease
(Goodpasture's syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Eye, disease
Graves' disease
(Graves' ophthalmopathy; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Nervous system, disease
(Guillain-Barre syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Ear, disease
(Meniere's; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Skin, neoplasm
(Sezary syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Skin, neoplasm
(T-cell lymphoma; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Disease, animal
(Vogt-Koyanagi-Harada's syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Granulomatous disease
(Wegener's granulomatosis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Infection
(acute hepatitis B; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Edema
(angioneurotic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Antiarteriosclerotics
(antiatherosclerotics; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Erythropoiesis
(aplasia; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Anemia (disease)
(aplastic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Alopecia

- (areata; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Dermatitis
 - (atopic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Chemotherapy
 - (augmentation of; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Anemia (disease)
 - Autoimmune disease
 - (autoimmune hemolytic anemia; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Autoimmune disease
 - Inflammation
 - Thyroid gland, disease
 - (autoimmune thyroiditis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Hepatitis
 - (autoimmune; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Infection
 - (bacterial; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Cirrhosis
 - (biliary; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Bronchi, disease
 - Inflammation
 - (bronchitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Skin, disease
 - (bullous pemphigoid; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Inflammation
 - (carditis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Dermatitis
 - (contact; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Lymphoma
 - (cutaneous T-cell; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Connective tissue, disease
 - Inflammation
 - (eosinophilic fasciitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Skin, disease
 - (epidermolysis bullosa; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)
- IT Autoimmune disease
 - (exptl. autoimmune encephalomyelitis; preparation of amino functionalized organo phosphonates or organo carboxylates as

- SiP1/Edg1 receptor agonists)
- IT Encephalomyelitis
(exptl. autoimmune; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Kidney, disease
(failure, acute, ischemic; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Kidney, disease
(failure, chronic; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Liver, disease
(failure; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Digestive tract, disease
Inflammation
(gastroenteritis, eosinophilic; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Gingiva, disease
Inflammation
(gingivitis; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Inflammation
Kidney, disease
(glomerulonephritis; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Hair preparations
(growth stimulants; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Kidney, disease
(hemolytic-uremic syndrome; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Eye, disease
Infection
Inflammation
(herpetic keratitis; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Skin, disease
(hyperproliferation; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Skin, disease
(ichthyosis; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Purpura (disease)
(idiopathic thrombocytopenic; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Intestine, disease
(inflammatory; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)
- IT Inflammation
Kidney, disease
(interstitial nephritis; preparation of amino functionalized organo phosphonates or organo carboxylates as SiP1/Edg1 receptor agonists)

- IT Pneumonia
 (interstitial; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Eye, disease
 Inflammation
 (keratitis; preparation of amino functionalized organo phosphonates
 or organo carboxylates as S1P1/Edg1
 receptor agonists)
- IT Eye, disease
 Inflammation
 (keratoconjunctivitis; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Skin, disease
 (lichen planus; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Necrosis
 (liver, acute; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Eye, disease
 (macula, senile degeneration; preparation of amino functionalized
 organo phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Anemia (disease)
 (megaloblastic anemia; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Carcinoma
 (metastasis; preparation of amino functionalized organo phosphonates
 or organo carboxylates as S1P1/Edg1
 receptor agonists)
- IT Headache
 (migraine; preparation of amino functionalized organo phosphonates
 or organo carboxylates as S1P1/Edg1
 receptor agonists)
- IT Erythema
 (multiforme; preparation of amino functionalized organo phosphonates
 or organo carboxylates as S1P1/Edg1
 receptor agonists)
- IT Heart, disease
 Inflammation
 (myocarditis; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Liver, disease
 (necrosis, acute; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Inflammation
 Nerve, disease
 (neuritis; preparation of amino functionalized organo phosphonates
 or organo carboxylates as S1P1/Edg1
 receptor agonists)
- IT Hepatitis
 (non-A, non-B; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Inflammation
 Pancreas, disease
 (pancreatitis; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
- IT Skin, disease
 (pemphigus foliaceus; preparation of amino functionalized organo

phosphonates or organo carboxylates as S1P1/
Edg1 receptor agonists)

IT Artery, disease
Inflammation
(periarteritis nodosa; preparation of amino functionalized organo
phosphonates or organo carboxylates as S1P1/
Edg1 receptor agonists)

IT Inflammation
Periodontium, disease
(periodontitis; preparation of amino functionalized organo
phosphonates or organo carboxylates as S1P1/
Edg1 receptor agonists)

IT Anemia (disease)
(pernicious anemia; preparation of amino functionalized organo
phosphonates or organo carboxylates as S1P1/
Edg1 receptor agonists)

IT Allergy
(photoallergic contact dermatitis; preparation of amino
functionalized organo phosphonates or organo carboxylates as
S1P1/Edg1 receptor agonists)

IT Dermatitis
(photoallergic contact; preparation of amino functionalized organo
phosphonates or organo carboxylates as S1P1/
Edg1 receptor agonists)

IT Allergy
(pollen; preparation of amino functionalized organo phosphonates or
organo carboxylates as S1P1/Edg1 receptor
agonists)

IT Myositis
(polymyositis; preparation of amino functionalized organo
phosphonates or organo carboxylates as S1P1/
Edg1 receptor agonists)

IT AIDS (disease)
Acne
Addison's disease
Aging, animal
Agranulocytosis
Allergy inhibitors
Anti-AIDS agents
Anti-inflammatory agents
Anti-ischemic agents
Antiartherosclerotics
Antiarthritics
Antiasthmatics
Antibacterial agents
Anticoagulants
Antidiabetic agents
Antihistamines
Antimigraine agents
Antitumor agents
Antiulcer agents
Arteriosclerosis
Asthma
Atherosclerosis
Behcet's syndrome
Blood coagulation
Celiac disease
Chronic lymphocytic leukemia
Cirrhosis
Dermatomyositis
Diabetes mellitus
Drug screening
Eczema
Emphysema
Eosinophilia
Erythema
Gingiva, disease

Graves' disease
 Human
 Hyperthyroidism
 Hypoxia
 Immunosuppressants
 Ischemia
 Leukotriene antagonists
 Lung, neoplasm
 Lymphocytic leukemia
 Lymphoma
 Mastocytoma
 Multiple sclerosis
 Muscular dystrophy
 Myasthenia gravis
 Myositis
 Nervous system agents
 Osteoporosis
 Periodontium
 Psoriasis
 Rheumatic fever
 Rheumatoid arthritis
 Sarcoidosis
 Sepsis
 Sjogren syndrome
 Transformation, neoplastic
 Transplant rejection
 Urticaria
 (preparation of amino functionalized organo phosphonates or organo
 carboxylates as S1P1/Edg1 receptor
 agonists)
 IT Inflammation
 Intestine, disease
 (pseudomembranous enterocolitis; preparation of amino functionalized
 organo phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
 IT Skin, disease
 (pyoderma; preparation of amino functionalized organo phosphonates
 or organo carboxylates as S1P1/Edg1
 receptor agonists)
 IT Inflammation
 (rectal; preparation of amino functionalized organo phosphonates or
 organo carboxylates as S1P1/Edg1 receptor
 agonists)
 IT Intestine, disease
 (rectum, inflammation; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
 IT Eye, disease
 Inflammation
 (retinitis pigmentosa; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
 IT Inflammation
 Nose, disease
 (rhinitis; preparation of amino functionalized organo phosphonates
 or organo carboxylates as S1P1/Edg1
 receptor agonists)
 IT Connective tissue, disease
 (scleroderma; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
 IT Biliary tract, disease
 Inflammation
 (sclerosing cholangitis; preparation of amino functionalized organo
 phosphonates or organo carboxylates as S1P1/
 Edg1 receptor agonists)
 IT Mental and behavioral disorders

(senile psychosis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Shock (circulatory collapse)
(septic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Disease, animal
(siderosis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Lupus erythematosus
(systemic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Injury
(trauma; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Shock (circulatory collapse)
(traumatic; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Respiratory system, disease
(treatment; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Inflammation
Intestine, disease
(ulcerative colitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Eye, disease
Inflammation
(uveitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Blood vessel, disease
Inflammation
(vasculitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Infection
(viral hepatitis; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT Hepatitis
(viral; preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT 569684-52-2P 569684-61-3P 571206-20-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

IT 569682-66-2P 569682-67-3P 569682-68-4P
569682-69-5P 569682-70-8P 569682-71-9P
569682-72-0P 569682-73-1P 569682-74-2P
569682-75-3P 569682-77-5P 569682-78-6P
569682-79-7P 569682-80-0P 569682-81-1P 569682-82-2P
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569682-93-5P 569682-95-7P 569682-97-9P
569682-99-1P 569683-01-8P 569683-03-0P
569683-05-2P 569683-07-4P 569683-09-6P 569683-11-0P

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569683-13-2P 569683-15-4P 569683-17-6P 569683-21-2P
569683-23-4P 569683-25-6P 569683-27-8P 569683-28-9P
569683-30-3P 569683-32-5P 569683-34-7P
569683-39-2P 569683-41-6P 569683-43-8P
569683-45-0P 569683-47-2P 569683-49-4P
569683-51-8P 569683-55-2P 569683-57-4P
569683-59-6P 569683-61-0P 569683-63-2P
569683-67-6P 569683-68-7P 569683-70-1P
569683-72-3P 569683-74-5P 569683-76-7P
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570423-81-3P 571206-07-0P 571206-08-1P
571206-09-2P 571206-10-5P 571206-11-6P
571206-12-7P 571206-13-8P 571206-14-9P 571206-15-0P
571206-16-1P 571206-17-2P 571206-18-3P
571206-19-4P 571206-21-8P 571206-27-4P
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571206-37-6P 571206-38-7P 571206-40-1P
571206-41-2P 571206-42-3P 571206-43-4P
571206-44-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)

(preparation of amino functionalized organo phosphonates or organo
carboxylates as S1P1/Edg1 receptor
agonists)

IT 56-12-2, 4-Aminobutanoic acid, reactions 64-04-0, Phenethylamine
96-33-3, Methyl acrylate 98-80-6, Phenylboronic acid 100-83-4,
3-Hydroxybenzaldehyde 106-41-2, 4-Bromophenol 107-13-1,
Acrylonitrile, reactions 111-70-6, 1-Heptanol 111-86-4,
1-Octanamine 121-32-4, 3-Ethoxy-4-hydroxybenzaldehyde
121-33-5, 4-Hydroxy-3-methoxybenzaldehyde 123-08-0,

4-Hydroxybenzaldehyde 139-85-5, 3,4-Dihydroxybenzaldehyde
 143-16-8, Dihexylamine 350-92-5, 1,1,1-Trifluoro-3-
 phenyl-2-propanone 401-95-6, 3,5-Bis(trifluoromethyl)benzaldehyd
 e 542-69-8, 1-Iodobutane 556-18-3, 4-Aminobenzaldehyde
 589-29-7, 1,4-Benzenedimethanol 591-20-8, 3-Bromophenol
 619-66-9, 4-Formylbenzoic acid 623-27-8, Terephthalaldehyde
 629-27-6, 1-Iodoctane 637-59-2, 1-Bromo-3-phenylpropane
 638-45-9, 1-Iodohexane 682-30-4, Diethyl vinylphosphonate
 924-49-2, 4-Amino-3-hydroxybutanoic acid 2052-07-5,
 2-Bromobiphenyl 2113-57-7, 3-Bromobiphenyl 2233-18-3,
 4-Hydroxy-3,5-dimethylbenzaldehyde 2314-36-5,
 3,5-Dichloro-4-hydroxybenzaldehyde 2374-05-2,
 4-Bromo-2,6-dimethylphenol 2420-16-8, 3-Chloro-4-
 hydroxybenzaldehyde 2439-54-5, N-Methyloctylamine 2495-35-4,
 Benzyl acrylate 2973-76-4, 3-Bromo-4-hydroxy-5-
 methoxybenzaldehyde 2973-77-5, 3,5-Dibromo-4-
 hydroxybenzaldehyde 2973-78-6, 3-Bromo-4-hydroxybenzaldehyde
 3111-37-3, 3-Bromo-5-ethoxy-4-hydroxybenzaldehyde 3132-99-8,
 3-Bromobenzaldehyde 3261-62-9, 4-Methylphenethylamine
 3300-51-4, 4-Trifluoromethylbenzylamine 3453-33-6,
 6-Methoxy-2-naphthaldehyde 3761-92-0, Hexylmagnesium bromide
 3964-56-5, 4-Bromo-2-chlorophenol 4282-40-0, 1-Iodoheptane
 4282-42-2, 1-Iodononane 4282-44-4, 1-Iodoundecane 4815-96-7,
 3-Bromo-5-benzyloxy-4-hydroxybenzaldehyde 5438-36-8,
 4-Hydroxy-3-iodo-5-methoxybenzaldehyde 6138-90-5, Geranyl
 bromide 6323-99-5 7368-78-7, 4-Bromo-2-methoxyphenol
 7463-51-6, 4-Bromo-3,5-dimethylphenol 7530-27-0,
 4-Bromo-2-chloro-6-methylphenol 7770-45-8, 4-Hydroxy-1-
 naphthaldehyde 10521-91-2, 5-Phenyl-1-pentanol 13138-33-5,
 3-Aminopropylphosphonic acid 13214-66-9, Benzenebutanamine
 13477-53-7, 4-Amino-2-hydroxybutanoic acid 13631-21-5,
 4-Bromo-3-chlorophenol 13880-74-5, 4-Aminopentanoic acid
 15174-69-3, 4-Hydroxy-3-methylbenzaldehyde 18278-34-7,
 4-Hydroxy-2-methoxybenzaldehyde 19463-48-0, 3-Chloro-4-hydroxy-5-
 methoxybenzaldehyde 23703-22-2, 1-Bromo-4-hexylbenzene
 25006-17-1, 4-Hydroxy-3-methoxy-5-propylbenzaldehyde 35622-27-6,
 4-Aminobutylphosphonic acid 36476-78-5,
 3-Azetidinecarboxylic acid 38841-98-4, Octylmagnesium chloride
 40499-83-0, 3-Pyrrolidinol 50773-56-3, 3-Benzyloxy-4-
 hydroxybenzaldehyde 51572-88-4, 4-Formyl-2-hydroxybenzoic acid
 54256-43-8, 4-Decylbenzoyl chloride 54963-70-1, 4-Nonylbenzoyl
 chloride 56217-93-7, 5-(3-Aminopropyl)-1H-tetrazole
 56962-11-9, 2-Chloro-4-hydroxybenzaldehyde 64283-87-0,
 4-Iodobutylbenzene 65564-05-8, 3-Benzyloxycarbonylaminopropanal
 65600-74-0, Ethyl diethoxymethylphosphinate 70547-87-4,
 4-Hydroxy-2,6-dimethylbenzaldehyde 76542-24-0,
 1-Bromo-4-nonylthiobenzene 87199-17-5, 4-Formylphenylboronic
 acid 93102-05-7 103680-71-3 130592-02-8,
 4-Amino-2,2-difluorobutanoic acid 148547-19-7, Methyl
 4-bromo-3-methylbenzoate 569684-89-5, 4-Amino-3-fluorobutanoic
 acid 569685-48-9 570424-08-7 570424-09-8
 570424-10-1 570424-11-2 570424-12-3
 571206-46-7, 4-Hydroxy-3-methoxy-5-propylthiobenzaldehyde
 571206-48-9, 4-Nonylbenzyl iodide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of amino functionalized organo phosphonates or organo
 carboxylates as S1P1/Edg1 receptor
 agonists)

IT 1203-68-5P, [1,1'-Biphenyl]-2-carboxaldehyde 1204-60-0P,
 [1,1'-Biphenyl]-3-carboxaldehyde 6853-57-2P 17012-21-4P
 24076-33-3P 24083-12-3P, 3-Octyloxybenzaldehyde 24083-13-4P,
 4-Octyloxybenzaldehyde 49763-67-9P 49763-69-1P 50262-46-9P
 54784-14-4P 56308-79-3P 59378-87-9P, 3-Pyrrolidinecarboxylic
 acid 60951-75-9P 61343-82-6P 62299-38-1P 70972-98-4P,
 4-Nonylbenzaldehyde 70972-99-5P, 4-Decylbenzaldehyde
 75472-36-5P 75677-08-6P 80407-63-2P 83697-65-8P
 101385-93-7P 101500-22-5P 103057-44-9P 103680-62-2P

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108898-23-3P 110943-74-3P 121118-78-3P 131888-48-7P
 146936-34-7P 149104-89-2P 167279-18-7P
 169806-13-7P 188846-99-3P 198959-37-4P
 208108-76-3P 246847-91-6P 256488-46-7P
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 571206-53-6P 571206-54-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)

(preparation of amino functionalized organo phosphonates or organo
 carboxylates as S1P1/Edg1 receptor
 agonists)

SEARCH

=> => d his 1119

(FILE 'HCAPLUS' ENTERED AT 12:23:02 ON 27 JUL 2007)

L119 0 S L117 NOT L101

=> d que 1119

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L2      424 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-83-4/BI OR
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        103680-62-2/BI OR 103680-71-3/BI OR 10521-91-2/BI OR
        106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
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        1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
        121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
        130592-02-8/BI OR 13138-33-5/BI OR 131888-48-7/BI OR
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        13880-74-5/BI OR 139-85-5/BI OR 143-16-8/BI OR
        146936-34-7/BI OR 148547-19-7/BI OR 149104-89-2/BI OR
        15174-69-3/BI OR 167279-18-7/BI OR 169806-13-7/BI OR
        17012-21-4/BI OR 18278-34-7/BI OR 188846-99-3/BI OR
        19463-48-0/BI OR 198959-37-4/BI OR 2052-07-5/BI OR
        208108-76-3/BI OR 2113-57-7/BI OR 2233-18-3/BI OR
        2314-36-5/BI OR 23703-22-2/BI OR 2374-05-2/BI OR
        24076-33-3/BI OR 24083-12-3/BI OR 24083-13-4/BI OR
        2420-16-8/BI OR 2439-54-5/BI OR 246847-91-6/BI OR
        2495-35-4/BI OR 25006-17-1/BI OR 256488-46-7/BI OR
        2973-76-4/BI OR 2973-77-5/BI OR 2973-78-6/BI OR
        3111-37-3/BI OR 3132-99-8/BI OR 3261-62-9/BI OR
        3300-51-4/BI OR 3453-33-6/BI OR 350-92-5/BI OR
        35622-27-6/BI OR 36476-78-5/BI OR 3761-92-0/BI OR
        38841-98-4/BI OR 3964-56-5/BI OR 401-95-6/BI OR
        40499-83-0/BI OR 4282-40-0/BI OR 4282-42-2/BI OR
        4282-44-4/BI OR 4815-96-7/BI OR 49763-67-9/BI OR
        49763-69-1/BI OR 500191-05-9/BI OR 50262-46-9/BI OR
        50773-56-3/BI OR 51572-88-4/BI OR 542-69-8/BI OR
        54256-43-8/BI OR 5438-36-8/BI OR 54784-14-4/BI OR
        54963-70-1/BI OR 556-18-3/BI OR 56-12-2/BI OR 56217-93-
        7/BI OR 56308-79-3/BI OR 56962-11-9/BI OR 569682-66-2/B
        I OR 569682-67-3/BI OR 569682-68-4/BI OR 569682-69-5/BI
        OR 569682-70-8/BI OR 569682-71-9/BI OR 569682-72-0/BI
        OR 569682-73-1/BI OR 569682-74-2/BI OR 569682-75-3/BI
        OR 569682-77-5/BI OR 569682-78-6/BI OR 569682-79-7/BI
        OR 569682-80-0/BI OR 569682-81-1/BI OR 569
L3      71 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/NR AND 1/P
        AND 1/N
L4      154 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/P
L6      23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND C4N/RF
L8      36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4S/RF
L9      67 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4N/RF
L10     7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND L9
L11     7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C2N2O/RF
L12     1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND L11
L13     43 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 3/F
L14     36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L8
L15     7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L10
L16     12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C3N/RF
L17     6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L8
L18     1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L11
L19     40 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND C6/RF AND
        2/NR
L20     9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L19 AND 4/O
L21     1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L20 AND C22 H33 N
        O4/MF
L22     2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND 1/F
L23     1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND 2/NR AND 2/O

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L24	22	SEA FILE=REGISTRY ABB=ON	PLU=ON	L9 AND 2/NR AND 2-3/O AND C6/RF
L25	11	SEA FILE=REGISTRY ABB=ON	PLU=ON	L24 AND 2/O
L26	2	SEA FILE=REGISTRY ABB=ON	PLU=ON	L25 AND 21/C
L27	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	L24 AND 20/C AND 3/O
L28	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	L2 AND 2/BR
L29	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	L28 AND 2/NR
L30	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	L9 AND 2/NR AND 5/O AND 1/P
L31	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	L15 AND 4/NR
L32	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	L31 AND 3/O
L33	27	SEA FILE=REGISTRY ABB=ON	PLU=ON	L3 AND 4/O
L34	10	SEA FILE=REGISTRY ABB=ON	PLU=ON	L2 AND ?NAPHTH?/CNS
L35	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	L34 AND 20-30/C
L37	44	SEA FILE=REGISTRY ABB=ON	PLU=ON	L2 AND ?BIPHENYL?/CNS
L38	32	SEA FILE=REGISTRY ABB=ON	PLU=ON	L37 AND 20-100/C
L41	68	SEA FILE=REGISTRY ABB=ON	PLU=ON	L3 AND C6/RF
L42	68	SEA FILE=REGISTRY ABB=ON	PLU=ON	L41 AND 12-50/C
L43	157	SEA FILE=REGISTRY ABB=ON	PLU=ON	L6 OR (L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35 OR L38
L44	199	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L41 OR L42 OR L43)
L48		QUE ABB=ON	PLU=ON	PY<2003 OR PRY<2003 OR AY<2003 OR MY<2003 OR REVIEW/DT
L50		QUE ABB=ON	PLU=ON	IMMUNOSUPPRES? OR IMMUNOREG? OR IMMUN?(A) (SUPPRESS? OR REG?)
L52		QUE ABB=ON	PLU=ON	IMMUNOSUPPRESSANTS+PFT, OLD, NT/CT
L53		QUE ABB=ON	PLU=ON	IMMUNOSUPPRESSION+PFT, OLD, NT/CT
L55		QUE ABB=ON	PLU=ON	ANTAGONISM+PFT, OLD, NT/CT
L57		QUE ABB=ON	PLU=ON	AGON? OR ANTAG?
L59		QUE ABB=ON	PLU=ON	EDG1 (A) S1P?
L70		QUE ABB=ON	PLU=ON	"AUTOIMMUNE DISEASE"+PFT, OLD, NT/CT
L72		QUE ABB=ON	PLU=ON	INFLAMMATION+PFT, OLD, NT/CT
L74		QUE ABB=ON	PLU=ON	INFECTION+PFT, OLD, NT/CT
L76		QUE ABB=ON	PLU=ON	AIDS+PFT, OLD, NT/CT
L78		QUE ABB=ON	PLU=ON	ASTHMA+PFT, OLD, NT/CT
L80		QUE ABB=ON	PLU=ON	"RESPIRATORY SYSTEM, DISEASE"+PFT, OLD, NT/CT
L82		QUE ABB=ON	PLU=ON	ARTHRITIS+PFT, OLD, NT/CT
L84		QUE ABB=ON	PLU=ON	"MUSCULAR DYSTROPHY"+PFT, OLD, NT/CT
L86		QUE ABB=ON	PLU=ON	"SKIN, DISEASE"+PFT, OLD, NT/CT
L88		QUE ABB=ON	PLU=ON	DERMATITIS+PFT, OLD, NT/CT
L94		QUE ABB=ON	PLU=ON	NEOPLASM+PFT, OLD, NT/CT
L97	1272	SEA FILE=HCAPLUS ABB=ON	PLU=ON	("DOHERTY, GEORGE A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98		QUE ABB=ON	PLU=ON	MERCK?/PA, CS, SO, CO
L99	714	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L97 AND L48
L100	228	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L99 AND L98
L101	26	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L100 AND L50
L105	179	SEA FILE=REGISTRY ABB=ON	PLU=ON	L44 AND 18-70/C
L106	15	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L105
L109	20	SEA FILE=REGISTRY ABB=ON	PLU=ON	L44 NOT L105
L110	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	L109 AND C14 H24 N O4 P/MF
L111	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	L109 AND C17 H29 BR N O5 P/MF
L112	181	SEA FILE=REGISTRY ABB=ON	PLU=ON	L105 OR L110 OR L111
L113	15	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L112

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L114      15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L106 OR L113
L115      3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L114 AND L48
L116      3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L115 AND (L50 OR (L52
          OR L53) OR L55 OR L57 OR L59 OR L70 OR L72 OR L74 OR
          L76 OR L78 OR L80)
L117      3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L116 AND (L82 OR L84
          OR L86 OR L88 OR L94)
L119      0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L117 NOT L101
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=> d his 1121

(FILE 'HCAPLUS' ENTERED AT 12:23:02 ON 27 JUL 2007)

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L121      0 S L120 NOT L101
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=> d que 1121

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L2      424 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-83-4/BI OR
          101385-93-7/BI OR 101500-22-5/BI OR 103057-44-9/BI OR
          103680-62-2/BI OR 103680-71-3/BI OR 10521-91-2/BI OR
          106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
          110943-74-3/BI OR 111-70-6/BI OR 111-86-4/BI OR
          1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
          121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
          130592-02-8/BI OR 13138-33-5/BI OR 131888-48-7/BI OR
          13214-66-9/BI OR 13477-53-7/BI OR 13631-21-5/BI OR
          13880-74-5/BI OR 139-85-5/BI OR 143-16-8/BI OR
          146936-34-7/BI OR 148547-19-7/BI OR 149104-89-2/BI OR
          15174-69-3/BI OR 167279-18-7/BI OR 169806-13-7/BI OR
          17012-21-4/BI OR 18278-34-7/BI OR 188846-99-3/BI OR
          19463-48-0/BI OR 198959-37-4/BI OR 2052-07-5/BI OR
          208108-76-3/BI OR 2113-57-7/BI OR 2233-18-3/BI OR
          2314-36-5/BI OR 23703-22-2/BI OR 2374-05-2/BI OR
          24076-33-3/BI OR 24083-12-3/BI OR 24083-13-4/BI OR
          2420-16-8/BI OR 2439-54-5/BI OR 246847-91-6/BI OR
          2495-35-4/BI OR 25006-17-1/BI OR 256488-46-7/BI OR
          2973-76-4/BI OR 2973-77-5/BI OR 2973-78-6/BI OR
          3111-37-3/BI OR 3132-99-8/BI OR 3261-62-9/BI OR
          3300-51-4/BI OR 3453-33-6/BI OR 350-92-5/BI OR
          35622-27-6/BI OR 36476-78-5/BI OR 3761-92-0/BI OR
          38841-98-4/BI OR 3964-56-5/BI OR 401-95-6/BI OR
          40499-83-0/BI OR 4282-40-0/BI OR 4282-42-2/BI OR
          4282-44-4/BI OR 4815-96-7/BI OR 49763-67-9/BI OR
          49763-69-1/BI OR 500191-05-9/BI OR 50262-46-9/BI OR
          50773-56-3/BI OR 51572-88-4/BI OR 542-69-8/BI OR
          54256-43-8/BI OR 5438-36-8/BI OR 54784-14-4/BI OR
          54963-70-1/BI OR 556-18-3/BI OR 56-12-2/BI OR 56217-93-
          7/BI OR 56308-79-3/BI OR 56962-11-9/BI OR 569682-66-2/B
          I OR 569682-67-3/BI OR 569682-68-4/BI OR 569682-69-5/BI
          OR 569682-70-8/BI OR 569682-71-9/BI OR 569682-72-0/BI
          OR 569682-73-1/BI OR 569682-74-2/BI OR 569682-75-3/BI
          OR 569682-77-5/BI OR 569682-78-6/BI OR 569682-79-7/BI
          OR 569682-80-0/BI OR 569682-81-1/BI OR 569
L3      71 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/NR AND 1/P
          AND 1/N
L4      154 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/P
L6      23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND C4N/RF
L8      36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4S/RF
L9      67 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4N/RF
L10     7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND L9
L11     7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C2N2O/RF
L12     1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND L11
L13     43 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 3/F
L14     36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L8
L15     7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L13 AND L10
L16     12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C3N/RF
L17     6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L8
L18     1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND L11
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L19	40	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND C6/RF AND 2/NR
L20	9	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L19 AND 4/O
L21	1	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L20 AND C22 H33 N O4/MF
L22	2	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 1/F
L23	1	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L16 AND 2/NR AND 2/O
L24	22	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 2/NR AND 2-3/O AND C6/RF
L25	11	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L24 AND 2/O
L26	2	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L25 AND 21/C
L27	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L24 AND 20/C AND 3/O
L28	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND 2/BR
L29	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L28 AND 2/NR
L30	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 2/NR AND 5/O AND 1/P
L31	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L15 AND 4/NR
L32	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L31 AND 3/O
L33	27	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L3 AND 4/O
L34	10	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND ?NAPHTH?/CNS
L35	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L34 AND 20-30/C
L37	44	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND ?BIPHENYL?/CNS
L38	32	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L37 AND 20-100/C
L41	68	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L3 AND C6/RF
L42	68	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L41 AND 12-50/C
L43	157	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L6 OR (L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35 OR L38
L44	199	SEA FILE=REGISTRY	ABB=ON	PLU=ON	(L41 OR L42 OR L43)
L45	849	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L44
L46		QUE	ABB=ON	PLU=ON	PHARMAC?/SC, SX
L47	483	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L45 AND L46
L48		QUE	ABB=ON	PLU=ON	PY<2003 OR PRY<2003 OR AY<2003 OR MY<2003 OR REVIEW/DT
L49	270	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L47 AND L48
L50		QUE	ABB=ON	PLU=ON	IMMUNOSUPPRES? OR IMMUNOREG? OR IMMUN?(A) (SUPPRESS? OR REG?)
L51	7	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L50
L60	19	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	EDG1(A)S1P?
L61	2	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L60 AND L49
L68		QUE	ABB=ON	PLU=ON	AUTOIMMUN?
L69	21	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L68
L70		QUE	ABB=ON	PLU=ON	"AUTOIMMUNE DISEASE"+PFT, OLD, NT/CT
L71	32	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L70
L72		QUE	ABB=ON	PLU=ON	INFLAMMATION+PFT, OLD, NT/CT
L73	41	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L72
L74		QUE	ABB=ON	PLU=ON	INFECTION+PFT, OLD, NT/CT
L75	15	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L74
L76		QUE	ABB=ON	PLU=ON	AIDS+PFT, OLD, NT/CT
L77	7	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L76
L78		QUE	ABB=ON	PLU=ON	ASTHMA+PFT, OLD, NT/CT
L79	16	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L78
L80		QUE	ABB=ON	PLU=ON	"RESPIRATORY SYSTEM, DISEASE"+PFT, OLD, NT/CT
L81	29	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L80
L82		QUE	ABB=ON	PLU=ON	ARTHRITIS+PFT, OLD, NT/CT
L83	22	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L82
L84		QUE	ABB=ON	PLU=ON	"MUSCULAR DYSTROPHY"+PFT, OLD, NT/CT
L85	3	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L84
L86		QUE	ABB=ON	PLU=ON	"SKIN, DISEASE"+PFT, OLD, NT/CT
L87	30	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L86
L88		QUE	ABB=ON	PLU=ON	DERMATITIS+PFT, OLD, NT/CT

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L89      12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L88
L90      68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 OR L61 OR L69 OR
        L71 AND L73 OR L75 OR L77 OR L79 OR L81 OR L83 OR L85
        OR L89 OR L87
L94      QUE ABB=ON  PLU=ON  NEOPLASM+PFT,OLD,NT/CT
L95      44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L94
L96      32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L95 AND L90
L97      1272 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DOHERTY, GEORGE
        A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
        AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
        "MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
        "ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98      QUE ABB=ON  PLU=ON  MERCK?/PA,CS,SO,CO
L99      714 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L48
L100     228 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L99 AND L98
L101     26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L100 AND L50
L120     4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 AND L50
L121     0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L120 NOT L101
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=> d his 1122

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(FILE 'HCAPLUS' ENTERED AT 12:23:02 ON 27 JUL 2007)
L122     12 S L113 NOT (L118 OR L120)
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=> d que 1122

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L2      424 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-83-4/BI OR
        101385-93-7/BI OR 101500-22-5/BI OR 103057-44-9/BI OR
        103680-62-2/BI OR 103680-71-3/BI OR 10521-91-2/BI OR
        106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
        110943-74-3/BI OR 111-70-6/BI OR 111-86-4/BI OR
        1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
        121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
        130592-02-8/BI OR 13138-33-5/BI OR 131888-48-7/BI OR
        13214-66-9/BI OR 13477-53-7/BI OR 13631-21-5/BI OR
        13880-74-5/BI OR 139-85-5/BI OR 143-16-8/BI OR
        146936-34-7/BI OR 148547-19-7/BI OR 149104-89-2/BI OR
        15174-69-3/BI OR 167279-18-7/BI OR 169806-13-7/BI OR
        17012-21-4/BI OR 18278-34-7/BI OR 188846-99-3/BI OR
        19463-48-0/BI OR 198959-37-4/BI OR 2052-07-5/BI OR
        208108-76-3/BI OR 2113-57-7/BI OR 2233-18-3/BI OR
        2314-36-5/BI OR 23703-22-2/BI OR 2374-05-2/BI OR
        24076-33-3/BI OR 24083-12-3/BI OR 24083-13-4/BI OR
        2420-16-8/BI OR 2439-54-5/BI OR 246847-91-6/BI OR
        2495-35-4/BI OR 25006-17-1/BI OR 256488-46-7/BI OR
        2973-76-4/BI OR 2973-77-5/BI OR 2973-78-6/BI OR
        3111-37-3/BI OR 3132-99-8/BI OR 3261-62-9/BI OR
        3300-51-4/BI OR 3453-33-6/BI OR 350-92-5/BI OR
        35622-27-6/BI OR 36476-78-5/BI OR 3761-92-0/BI OR
        38841-98-4/BI OR 3964-56-5/BI OR 401-95-6/BI OR
        40499-83-0/BI OR 4282-40-0/BI OR 4282-42-2/BI OR
        4282-44-4/BI OR 4815-96-7/BI OR 49763-67-9/BI OR
        49763-69-1/BI OR 500191-05-9/BI OR 50262-46-9/BI OR
        50773-56-3/BI OR 51572-88-4/BI OR 542-69-8/BI OR
        54256-43-8/BI OR 5438-36-8/BI OR 54784-14-4/BI OR
        54963-70-1/BI OR 556-18-3/BI OR 56-12-2/BI OR 56217-93-
        7/BI OR 56308-79-3/BI OR 56962-11-9/BI OR 569682-66-2/B
        I OR 569682-67-3/BI OR 569682-68-4/BI OR 569682-69-5/BI
        OR 569682-70-8/BI OR 569682-71-9/BI OR 569682-72-0/BI
        OR 569682-73-1/BI OR 569682-74-2/BI OR 569682-75-3/BI
        OR 569682-77-5/BI OR 569682-78-6/BI OR 569682-79-7/BI
        OR 569682-80-0/BI OR 569682-81-1/BI OR 569
L3      71 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/NR AND 1/P
        AND 1/N
L4      154 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND 1/P
L6      23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND C4N/RF
L8      36 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND C4S/RF
```

L9	67	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND C4N/RF
L10	7	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L8 AND L9
L11	7	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND C2N2O/RF
L12	1	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L10 AND L11
L13	43	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND 3/F
L14	36	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L13 AND L8
L15	7	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L13 AND L10
L16	12	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND C3N/RF
L17	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L16 AND L8
L18	1	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L16 AND L11
L19	40	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND C6/RF AND 2/NR
L20	9	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L19 AND 4/O
L21	1	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L20 AND C22 H33 N O4/MF
L22	2	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 1/F
L23	1	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L16 AND 2/NR AND 2/O
L24	22	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 2/NR AND 2-3/O AND C6/RF
L25	11	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L24 AND 2/O
L26	2	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L25 AND 21/C
L27	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L24 AND 20/C AND 3/O
L28	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND 2/BR
L29	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L28 AND 2/NR
L30	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L9 AND 2/NR AND 5/O AND 1/P
L31	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L15 AND 4/NR
L32	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L31 AND 3/O
L33	27	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L3 AND 4/O
L34	10	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND ?NAPHTH?/CNS
L35	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L34 AND 20-30/C
L37	44	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L2 AND ?BIPHENYL?/CNS
L38	32	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L37 AND 20-100/C
L41	68	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L3 AND C6/RF
L42	68	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L41 AND 12-50/C
L43	157	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L6 OR (L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35 OR L38
L44	199	SEA FILE=REGISTRY	ABB=ON	PLU=ON	(L41 OR L42 OR L43)
L45	849	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L44
L46		QUE	ABB=ON	PLU=ON	PHARMAC?/SC, SX
L47	483	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L45 AND L46
L48		QUE	ABB=ON	PLU=ON	PY<2003 OR PRY<2003 OR AY<2003 OR MY<2003 OR REVIEW/DT
L49	270	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L47 AND L48
L50		QUE	ABB=ON	PLU=ON	IMMUNOSUPPRES? OR IMMUNOREG? OR IM MUN?(A) (SUPPRESS? OR REG?)
L51	7	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L50
L52		QUE	ABB=ON	PLU=ON	IMMUNOSUPPRESSANTS+PFT, OLD, NT/CT
L53		QUE	ABB=ON	PLU=ON	IMMUNOSUPPRESSION+PFT, OLD, NT/CT
L55		QUE	ABB=ON	PLU=ON	ANTAGONISM+PFT, OLD, NT/CT
L57		QUE	ABB=ON	PLU=ON	AGON? OR ANTAG?
L59		QUE	ABB=ON	PLU=ON	EDG1(A)S1P?
L60	19	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	EDG1(A)S1P?
L61	2	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L60 AND L49
L68		QUE	ABB=ON	PLU=ON	AUTOIMMUN?
L69	21	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L68
L70		QUE	ABB=ON	PLU=ON	"AUTOIMMUNE DISEASE"+PFT, OLD, NT/CT
L71	32	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L70
L72		QUE	ABB=ON	PLU=ON	INFLAMMATION+PFT, OLD, NT/CT
L73	41	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L49 AND L72
L74		QUE	ABB=ON	PLU=ON	INFECTION+PFT, OLD, NT/CT

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L75 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L74
L76 QUE ABB=ON PLU=ON AIDS+PFT,OLD,NT/CT
L77 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L76
L78 QUE ABB=ON PLU=ON ASTHMA+PFT,OLD,NT/CT
L79 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L78
L80 QUE ABB=ON PLU=ON "RESPIRATORY SYSTEM, DISEASE"+PFT,
OLD,NT/CT
L81 29 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L80
L82 QUE ABB=ON PLU=ON ARTHRITIS+PFT,OLD,NT/CT
L83 22 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L82
L84 QUE ABB=ON PLU=ON "MUSCULAR DYSTROPHY"+PFT,OLD,NT/CT
L85 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L84
L86 QUE ABB=ON PLU=ON "SKIN, DISEASE"+PFT,OLD,NT/CT
L87 30 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L86
L88 QUE ABB=ON PLU=ON DERMATITIS+PFT,OLD,NT/CT
L89 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L88
L90 68 SEA FILE=HCAPLUS ABB=ON PLU=ON L51 OR L61 OR L69 OR
L71 AND L73 OR L75 OR L77 OR L79 OR L81 OR L83 OR L85
OR L89 OR L87
L94 QUE ABB=ON PLU=ON NEOPLASM+PFT,OLD,NT/CT
L95 44 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND L94
L96 32 SEA FILE=HCAPLUS ABB=ON PLU=ON L95 AND L90
L97 1272 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DOHERTY, GEORGE
A."/AU OR "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/
AU OR "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR
"MANDALA, SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR
"ROSEN, HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
L98 QUE ABB=ON PLU=ON MERCK?/PA,CS,SO,CO
L99 714 SEA FILE=HCAPLUS ABB=ON PLU=ON L97 AND L48
L100 228 SEA FILE=HCAPLUS ABB=ON PLU=ON L99 AND L98
L101 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L100 AND L50
L103 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L96 NOT L101
L105 179 SEA FILE=REGISTRY ABB=ON PLU=ON L44 AND 18-70/C
L106 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L105
L109 20 SEA FILE=REGISTRY ABB=ON PLU=ON L44 NOT L105
L110 1 SEA FILE=REGISTRY ABB=ON PLU=ON L109 AND C14 H24 N
O4 P/MF
L111 1 SEA FILE=REGISTRY ABB=ON PLU=ON L109 AND C17 H29 BR
N O5 P/MF
L112 181 SEA FILE=REGISTRY ABB=ON PLU=ON L105 OR L110 OR L111

L113 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L112
L114 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L106 OR L113
L115 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L114 AND L48
L116 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L115 AND (L50 OR (L52
OR L53) OR L55 OR L57 OR L59 OR L70 OR L72 OR L74 OR
L76 OR L78 OR L80)
L117 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L116 AND (L82 OR L84
OR L86 OR L88 OR L94)
L118 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L117 NOT L103
L120 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L96 AND L50
L122 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L113 NOT (L118 OR
L120)

=> d his 1127

(FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 12:40:59 ON 27
JUL 2007)

L127 0 S L126

=> d que 1127

L2 424 SEA FILE=REGISTRY ABB=ON PLU=ON (100-83-4/BI OR
101385-93-7/BI OR 101500-22-5/BI OR 103057-44-9/BI OR
103680-62-2/BI OR 103680-71-3/BI OR 10521-91-2/BI OR
106-41-2/BI OR 107-13-1/BI OR 108898-23-3/BI OR
110943-74-3/BI OR 111-70-6/BI OR 111-86-4/BI OR

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1203-68-5/BI OR 1204-60-0/BI OR 121-32-4/BI OR
 121-33-5/BI OR 121118-78-3/BI OR 123-08-0/BI OR
 130592-02-8/BI OR 13138-33-5/BI OR 131888-48-7/BI OR
 13214-66-9/BI OR 13477-53-7/BI OR 13631-21-5/BI OR
 13880-74-5/BI OR 139-85-5/BI OR 143-16-8/BI OR
 146936-34-7/BI OR 148547-19-7/BI OR 149104-89-2/BI OR
 15174-69-3/BI OR 167279-18-7/BI OR 169806-13-7/BI OR
 17012-21-4/BI OR 18278-34-7/BI OR 188846-99-3/BI OR
 19463-48-0/BI OR 198959-37-4/BI OR 2052-07-5/BI OR
 208108-76-3/BI OR 2113-57-7/BI OR 2233-18-3/BI OR
 2314-36-5/BI OR 23703-22-2/BI OR 2374-05-2/BI OR
 24076-33-3/BI OR 24083-12-3/BI OR 24083-13-4/BI OR
 2420-16-8/BI OR 2439-54-5/BI OR 246847-91-6/BI OR
 2495-35-4/BI OR 25006-17-1/BI OR 256488-46-7/BI OR
 2973-76-4/BI OR 2973-77-5/BI OR 2973-78-6/BI OR
 3111-37-3/BI OR 3132-99-8/BI OR 3261-62-9/BI OR
 3300-51-4/BI OR 3453-33-6/BI OR 350-92-5/BI OR
 35622-27-6/BI OR 36476-78-5/BI OR 3761-92-0/BI OR
 38841-98-4/BI OR 3964-56-5/BI OR 401-95-6/BI OR
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 OR 569682-77-5/BI OR 569682-78-6/BI OR 569682-79-7/BI
 OR 569682-80-0/BI OR 569682-81-1/BI OR 569

L3	71	SEA FILE=REGISTRY ABB=ON PLU=ON	L2 AND 1/NR AND 1/P AND 1/N
L4	154	SEA FILE=REGISTRY ABB=ON PLU=ON	L2 AND 1/P
L6	23	SEA FILE=REGISTRY ABB=ON PLU=ON	L4 AND C4N/RF
L8	36	SEA FILE=REGISTRY ABB=ON PLU=ON	L2 AND C4S/RF
L9	67	SEA FILE=REGISTRY ABB=ON PLU=ON	L2 AND C4N/RF
L10	7	SEA FILE=REGISTRY ABB=ON PLU=ON	L8 AND L9
L11	7	SEA FILE=REGISTRY ABB=ON PLU=ON	L2 AND C2N2O/RF
L12	1	SEA FILE=REGISTRY ABB=ON PLU=ON	L10 AND L11
L13	43	SEA FILE=REGISTRY ABB=ON PLU=ON	L2 AND 3/F
L14	36	SEA FILE=REGISTRY ABB=ON PLU=ON	L13 AND L8
L15	7	SEA FILE=REGISTRY ABB=ON PLU=ON	L13 AND L10
L16	12	SEA FILE=REGISTRY ABB=ON PLU=ON	L2 AND C3N/RF
L17	6	SEA FILE=REGISTRY ABB=ON PLU=ON	L16 AND L8
L18	1	SEA FILE=REGISTRY ABB=ON PLU=ON	L16 AND L11
L19	40	SEA FILE=REGISTRY ABB=ON PLU=ON	L9 AND C6/RF AND 2/NR
L20	9	SEA FILE=REGISTRY ABB=ON PLU=ON	L19 AND 4/O
L21	1	SEA FILE=REGISTRY ABB=ON PLU=ON	L20 AND C22 H33 N O4/MF
L22	2	SEA FILE=REGISTRY ABB=ON PLU=ON	L9 AND 1/F
L23	1	SEA FILE=REGISTRY ABB=ON PLU=ON	L16 AND 2/NR AND 2/O
L24	22	SEA FILE=REGISTRY ABB=ON PLU=ON	L9 AND 2/NR AND 2-3/O AND C6/RF
L25	11	SEA FILE=REGISTRY ABB=ON PLU=ON	L24 AND 2/O
L26	2	SEA FILE=REGISTRY ABB=ON PLU=ON	L25 AND 21/C
L27	4	SEA FILE=REGISTRY ABB=ON PLU=ON	L24 AND 20/C AND 3/O
L28	6	SEA FILE=REGISTRY ABB=ON PLU=ON	L2 AND 2/BR
L29	3	SEA FILE=REGISTRY ABB=ON PLU=ON	L28 AND 2/NR
L30	6	SEA FILE=REGISTRY ABB=ON PLU=ON	L9 AND 2/NR AND 5/O AND 1/P
L31	6	SEA FILE=REGISTRY ABB=ON PLU=ON	L15 AND 4/NR
L32	5	SEA FILE=REGISTRY ABB=ON PLU=ON	L31 AND 3/O
L33	27	SEA FILE=REGISTRY ABB=ON PLU=ON	L3 AND 4/O

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L34      10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?NAPHTH?/CNS
L35      5  SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 AND 20-30/C
L37      44 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND ?BIPHENYL?/CNS

L38      32 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37 AND 20-100/C
L41      68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND C6/RF
L42      68 SEA FILE=REGISTRY ABB=ON  PLU=ON  L41 AND 12-50/C
L43      157 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR (L10 OR L11 OR
        L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18) OR (L19
        OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR
        L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33) OR L35
        OR L38
L44      199 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L41 OR L42 OR L43)
L105     179 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 AND 18-70/C
L109     20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44 NOT L105
L110     1  SEA FILE=REGISTRY ABB=ON  PLU=ON  L109 AND  C14 H24 N
        O4 P/MF
L111     1  SEA FILE=REGISTRY ABB=ON  PLU=ON  L109 AND  C17 H29 BR
        N O5 P/MF
L112     181 SEA FILE=REGISTRY ABB=ON  PLU=ON  L105 OR L110 OR L111

L126     0  SEA FILE=REGISTRY ABB=ON  PLU=ON  L112 AND EMBASE/LC
L127     0  SEA L126
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=> dup rem l119 l121 l122 l127

L119 HAS NO ANSWERS

L121 HAS NO ANSWERS

L127 HAS NO ANSWERS

FILE 'HCAPLUS' ENTERED AT 13:06:51 ON 27 JUL 2007

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FILE COVERS 1907 - 27 Jul 2007 VOL 147 ISS 6

FILE LAST UPDATED: 26 Jul 2007 (20070726/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

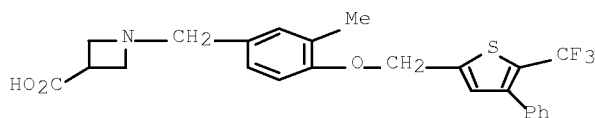
PROCESSING COMPLETED FOR L119

PROCESSING COMPLETED FOR L121

PROCESSING COMPLETED FOR L122

PROCESSING COMPLETED FOR L127

L134 12 DUP REM L119 L121 L122 L127 (0 DUPLICATES REMOVED)
 ANSWERS '1-12' FROM FILE HCAPLUS



10/501176

402615-91-2, FTY720-P 570423-80-2 635701-59-6

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(identification of Leu276 of S1P1 receptor and Phe263 of S1P3 receptor in interaction with receptor specific agonists by mol. modeling, site-directed mutagenesis, and affinity studies)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1311129 HCAPLUS Full-text

DOCUMENT NUMBER: 146:62699

TITLE: Preparation of polycyclic oxadiazoles or isoxazoles as S1P receptor ligands

INVENTOR(S): Albert, Rainer; Weiler, Sven; Zecri, Frederic

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 53pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2006131336	A1	20061214	WO 2006-EP5422	

2006

0607

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2005-11684 A

2005

0608

GB 2005-25064 A

2005

1208

GB 2006-405 A

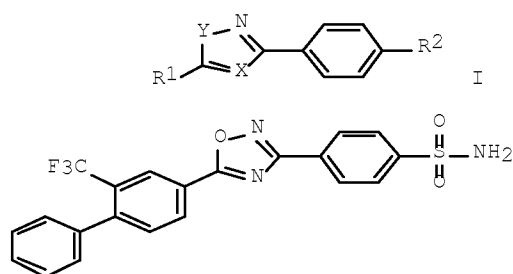
2006

0110

OTHER SOURCE(S): MARPAT 146:62699

ED Entered STN: 15 Dec 2006

GI



AB Title compds. represented by the formula I [wherein X = -N=, Y = O; X = -O-, Y = -N=; R1 = substituted biphenyl, 4-phenoxyphenyl or 4-(phenylalkoxy)phenyl; R2 = (un)substituted alkyl, amino, sulfamoyl, etc.; and physiol. hydrolyzable derivs., hydrates or solvates thereof] were prepared as sphingosine-1-phosphate (S1P) receptor ligands. For example, II was provided in a multi-step synthesis starting from 4-chloro-3-trifluoromethylbenzoic acid. I showed binding affinity to human S1P1 receptor with EC50 < 1 nM, are active in in vitro FLIPR calcium flux assay at a concentration of from 10⁻¹²-3.10⁻⁵ nM, and have EC50 of less than 10 mg/kg in in vivo screening assays for measurement of blood lymphocyte depletion. Thus, I and their pharmaceutical compns. are useful as S1P receptor ligands, particularly as immunosuppressants.

IT 569685-50-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

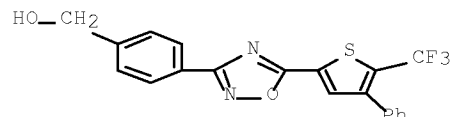
THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(preparation of polycyclic oxadiazoles or isoxazoles as S1P receptor ligands)

RN 569685-50-3 HCAPLUS

CN Benzenemethanol, 4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]- (CA INDEX NAME)



CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT	569685-50-3P	916804-38-1P	916804-44-9P	916804-47-2P
	916804-50-7P	916804-53-0P	916804-57-4P	916804-70-1P
	916804-77-8P	916804-85-8P	916804-91-6P	916804-98-3P
	916805-01-1P	916805-05-5P	916805-07-7P	916805-09-9P
	916805-11-3P	916805-13-5P	916805-15-7P	916805-16-8P
	916805-17-9P	916805-18-0P	916805-19-1P	916805-20-4P
	916805-21-5P	916805-22-6P	916805-23-7P	916805-24-8P
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	916805-29-3P	916805-30-6P	916805-31-7P	916805-32-8P
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10/501176

916805-73-7P	916805-74-8P	916805-75-9P	916805-76-0P
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916806-80-9P	916806-81-0P	916806-82-1P	916806-83-2P
916806-84-3P	916806-85-4P	916833-78-8P	916833-79-9P
916833-80-2P	916833-81-3P		

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)

(preparation of polycyclic oxadiazoles or isoxazoles as 51P receptor
 ligands)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT

L134 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:818237 HCAPLUS Full-text

DOCUMENT NUMBER: 145:224859

TITLE: Antilymphocyte antibody induction for
 prevention of transplant rejection

INVENTOR(S): Aradhya, Shreeram

PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH

SOURCE: PCT Int. Appl., 21pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	
WO 2006086361	A2	20060817	WO 2006-US4234	2006 0206
WO 2006086361	A3	20070118		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
 CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG,
 ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
 KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
 LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ,
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
 SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW

10/501176

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL,
SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2005-651045P

P

2005

0208

ED Entered STN: 17 Aug 2006

AB An immunosuppressive treatment combining a S1P receptor modulator, one or more immunosuppressive drug(s) and an antilymphocyte antibody in the course of the treatment of a transplant recipient prolongs the survival of a transplant allograft. Thus, the patients were administered (i) FTY720 5 mg given 2 to 12 h prior to renal allograft revascularization, then 2.5 mg daily, (ii) cyclosporine A 8 to 10 mg/kg/day adjusted to achieve target blood levels, and (iii) corticosteroids. The dosage regimen of the study had a beneficial effect compared to standard immunosuppressive regimens.

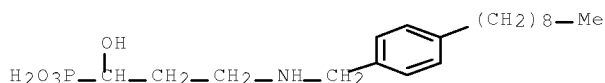
IT 569684-46-4 569684-82-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antilymphocyte antibody in combination with immunosuppressant and S1P receptor modulator for prevention of transplant rejection)

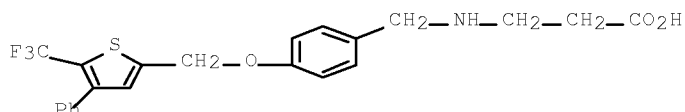
RN 569684-46-4 HCAPLUS

CN Phosphonic acid, [1-hydroxy-3-[[4-(nonylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569684-82-8 HCAPLUS

CN β-Alanine, N-[[4-[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



CC 1-7 (Pharmacology)

Section cross-reference(s): 15, 63

IT 24280-93-1, Mycophenolic acid 59865-13-3, Cyclosporine A

162359-56-0, FTY 720 569684-46-4 569684-82-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antilymphocyte antibody in combination with immunosuppressant and S1P receptor modulator for prevention of transplant rejection)

L134 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:677741 HCAPLUS Full-text

DOCUMENT NUMBER: 145:117363

TITLE: Use of sphingosine-1-phosphate (S1P) receptor agonists for the treatment of hepatitis C virus (HCV) disorders

INVENTOR(S): Brinkmann, Volker; Feutren, Gilles

PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH

10/501176

SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
----- ----- WO 2006072562	----- ----- A1	----- ----- 20060713	----- ----- WO 2006-EP3	2006 0102

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
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 ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
 KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
 LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ,
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
 SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI,
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
 NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL,
 SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2005-20 A 2005
 0104

OTHER SOURCE(S): MARPAT 145:117363

ED Entered STN: 13 Jul 2006

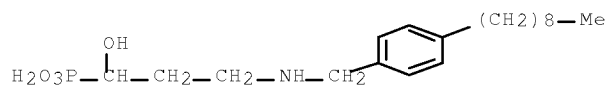
AB S1P receptor agonists are useful for the treatment of hepatitis C or chronic hepatitis C (HCV).

IT 569684-46-4 569684-82-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (S1P receptor agonists for treatment of hepatitis C virus
 disorders)

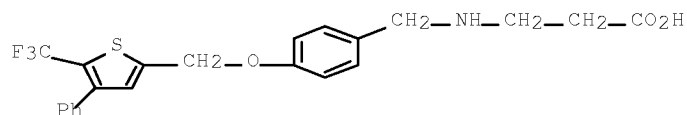
RN 569684-46-4 HCAPLUS

CN Phosphonic acid, [1-hydroxy-3-[[4-(nonylphenyl)methyl]amino]propyl
]- (9CI) (CA INDEX NAME)



RN 569684-82-8 HCAPLUS

CN β -Alanine, N-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



CC 1-5 (Pharmacology)

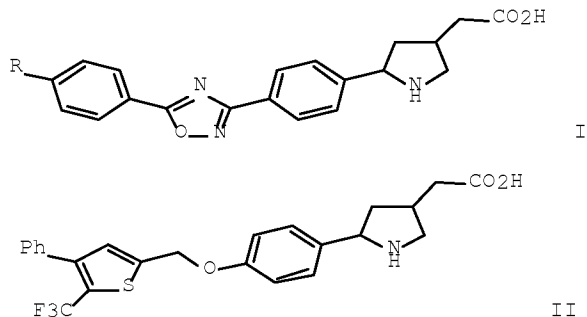
IT 569684-46-4 569684-82-8

10/501176

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(S1P receptor agonists for treatment of hepatitis C virus
disorders)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L134 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:499151 HCAPLUS Full-text
DOCUMENT NUMBER: 145:145483
TITLE: 2-Aryl(pyrrolidin-4-yl)acetic acids are potent
agonists of sphingosine-1-phosphate (S1P)
receptors
AUTHOR(S): Yan, Lin; Budhu, Richard; Huo, Pei; Lynch,
Christopher L.; Hale, Jeffrey J.; Mills,
Sander G.; Hajdu, Richard; Keohane, Carol A.;
Rosenbach, Mark J.; Milligan, James A.; Shei,
Gan-Ju; Chrebet, Gary; Bergstrom, James; Card,
Deborah; Mandala, Suzanne M.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck
Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters
(2006), 16(13), 3564-3568
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:145483
ED Entered STN: 29 May 2006
GI



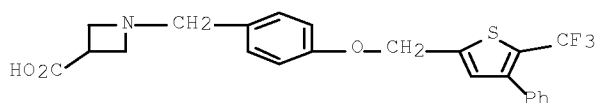
AB 2-Aryl(pyrrolidin-4-yl)acetic acids I [R = i-Bu, cyclopentyl, cyclohexyl, F3C(CH2)2,
3,3-difluoro-1-cyclopentyl, 4,4-difluoro-1-cyclohexyl] and II were synthesized and
their biol. activities as agonists of S1P receptors were evaluated. These analogs were
able to induce lowering of lymphocyte counts in the peripheral blood of mice and were
found to have good overall pharmacokinetic properties in rats.

IT 570423-67-5

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL
(Biological study)
(preparation and biol. activity of thiophene- or
oxadiazole-functionalized (aryl)pyrrolidineacetic acids as
potent agonists of sphingosine-1-phosphate receptors)

RN 570423-67-5 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-
thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 28

IT 570423-67-5 635701-59-6

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)

(preparation and biol. activity of thiophene- or oxadiazole-functionalized (aryl)pyrrolidineacetic acids as potent agonists of sphingosine-1-phosphate receptors)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:772794 HCAPLUS Full-text

DOCUMENT NUMBER: 145:369215

TITLE: Species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist in rats and dogs: formation of a unique glutathione adduct in the rat

AUTHOR(S): Anari, M. Reza; Creighton, Melissa D.; Ngui, Jason S.; Tschirret-Guth, Richard A.; Teffera, Yohannes; Doss, George A.; Tang, Wei; Yu, Nathan X.; Ciccotto, Suzanne L.; Hobra, Donald F., Jr.; Coleman, John B.; Vincent, Stella H.; Evans, David C.

CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, West Point, PA, USA

SOURCE: Drug Metabolism and Disposition (2006), 34(8), 1367-1375

CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 06 Aug 2006

AB The pharmacokinetics and metabolism of 1-((4-((4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy)benzyl)azetidine-3-carboxylic acid (MRL-A), a selective agonist for the sphingosine-1-phosphate 1 (S1P1) receptor, were investigated in rats and dogs. In both species, more than 50% of the dose was excreted in bile. Specific to the rat, and observed in bile, were a taurine conjugate of MRL-A and a glucuronide conjugate of an azetidine lactam metabolite. In dogs, a smaller portion of the dose (54% of administered dose) was excreted intact in bile, and the major metabolites detected were an azetidine N-oxide of MRL-A and an acylglucuronide of an N-dealkylation product. This latter metabolite was also observed in rat bile. Stereoselective formation of the N-oxide isomer was observed in dogs, whereas the rat produced comparable amts. of both isomers. The formation of a unique glutathione adduct was observed in rat bile, which was proposed to occur via N-dealkylation, followed by reduction of the putative aldehyde product to form the alc., and dehydration of the alc. to generate a reactive quinone methide intermediate. Incubation of a synthetic standard of this alc. in rat microsomes fortified with reduced glutathione or rat hepatocytes resulted in formation of this unique glutathione adduct.

IT 570423-67-5, MRL-A

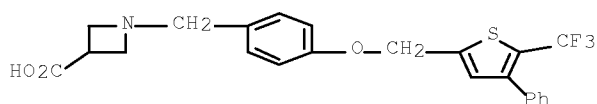
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)

RN 570423-67-5 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-

10/501176

thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



CC 1-2 (Pharmacology)

IT 570423-67-5, MRL-A

RL: PKT (Pharmacokinetics); BIOL (Biological study)
(species differences in metabolism and pharmacokinetics of a
sphingosine-1-phosphate receptor agonist MRL-A in rats and
dogs)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L134 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:986123 HCAPLUS Full-text

DOCUMENT NUMBER: 143:431986

TITLE: Discovery of Potent 3,5-Diphenyl-1,2,4-
oxadiazole Sphingosine-1-phosphate-1 (S1P1)
Receptor Agonists with Exceptional Selectivity
against S1P2 and S1P3

AUTHOR(S): Li, Zhen; Chen, Weirong; Hale, Jeffrey J.;
Lynch, Christopher L.; Mills, Sander G.;
Hajdu, Richard; Keohane, Carol Ann; Rosenbach,
Mark J.; Milligan, James A.; Shei, Gan-Ju;
Chrebet, Gary; Parent, Stephen A.; Bergstrom,
James; Card, Deborah; Forrest, Michael;
Quackenbush, Elizabeth J.; Wickham, L.
Alexandra; Vargas, Hugo; Evans, Rose M.;
Rosen, Hugh; Mandala, Suzanne

CORPORATE SOURCE: Departments of Medicinal Chemistry and
Immunology Rheumatology Research, Merck
Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Journal of Medicinal Chemistry (2005), 48(20),
6169-6173

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:431986

ED Entered STN: 11 Sep 2005

AB A class of 3,5-diphenyl-1,2,4-oxadiazole based compds. have been identified as potent
sphingosine-1-phosphate-1 (S1P1) receptor agonists with minimal affinity for the S1P2
and S1P3 receptor subtypes. Analog 26 (S1P1 IC50 = 0.6 nM) has an excellent
pharmacokinetics profile in the rat and dog and is efficacious in a rat skin transplant
model, indicating that S1P3 receptor agonism is not a component of immunosuppressive
efficacy.

IT 570423-67-5 570423-80-2

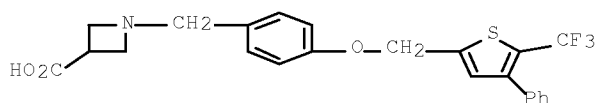
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole
Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with
Exceptional Selectivity)

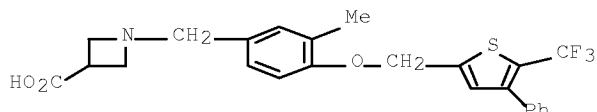
RN 570423-67-5 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-
thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

10/501176

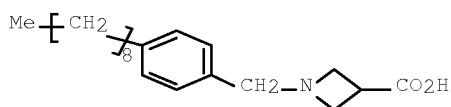


RN 570423-80-2 HCAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)



CC 1-3 (Pharmacology)
Section cross-reference(s): 28
IT 159222-57-8 162359-55-9 402615-91-2 570423-67-5
570423-80-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with Exceptional Selectivity)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1048937 HCAPLUS Full-text
DOCUMENT NUMBER: 142:147835
TITLE: A Rational Utilization of High-Throughput Screening Affords Selective, Orally Bioavailable 1-Benzyl-3-carboxyazetidine Sphingosine-1-phosphate-1 Receptor Agonists
AUTHOR(S): Hale, Jeffrey J.; Lynch, Christopher L.; Neway, William; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Parent, Stephen A.; Chrebet, Gary; Bergstrom, James; Card, Deborah; Ferrer, Marc; Hodder, Peter; Strulovici, Berta; Rosen, Hugh; Mandala, Suzanne
CORPORATE SOURCE: Departments of Medicinal Chemistry and Immunology and Rheumatology Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(27), 6662-6665
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:147835
ED Entered STN: 08 Dec 2004
GI



I

AB Moderately potent, selective S1P1 receptor agonists identified from high-throughput screening have been adapted into lipophilic tails for a class of orally bioavailable amino acid-based S1P1 agonists represented by I. Many of the new compds. are potent S1P1 agonists that select against the S1P2, S1P3, and S1P4 (although not S1P5) receptor subtypes. Two of the analogs are highly orally bioavailable and possess excellent pharmacokinetic profiles in the rat, dog, and rhesus monkey.

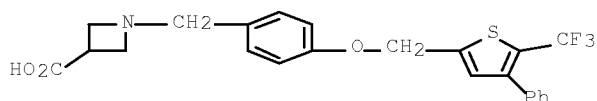
IT 570423-67-5P 570423-76-6P 570423-80-2P
570423-81-3P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)

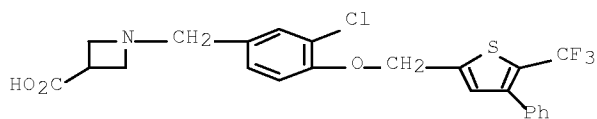
RN 570423-67-5 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



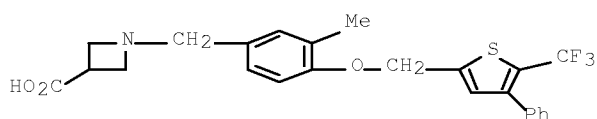
RN 570423-76-6 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

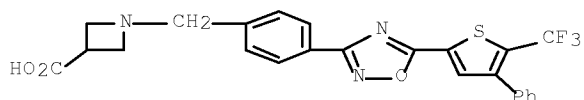


RN 570423-80-2 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)

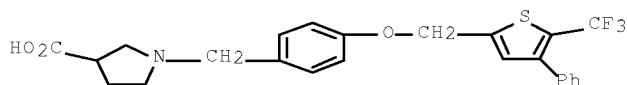


RN 570423-81-3 HCAPLUS
 CN 3-Azetidinecarboxylic acid, 1-[[4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]phenyl]methyl]- (9CI) (CA INDEX NAME)

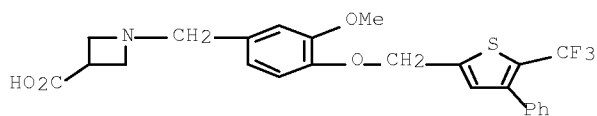


IT 570423-45-9P 570423-78-8P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)

RN 570423-45-9 HCAPLUS
 CN 3-Pyrrolidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



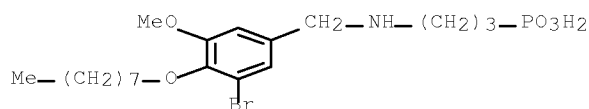
RN 570423-78-8 HCAPLUS
 CN 3-Azetidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



IT 569683-55-2 570423-38-0 570423-46-0
 570423-68-6
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)

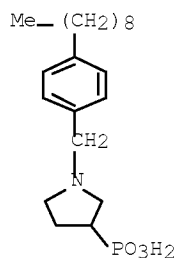
RN 569683-55-2 HCAPLUS
 CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)

10/501176



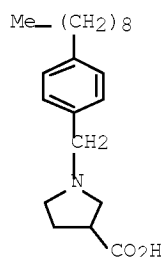
RN 570423-38-0 HCAPLUS

CN Phosphonic acid, [1-[(4-nonylphenyl)methyl]-3-pyrrolidinyl]- (9CI)
(CA INDEX NAME)



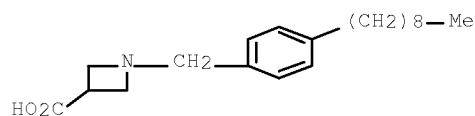
RN 570423-46-0 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[(4-nonylphenyl)methyl]- (9CI)
(CA INDEX NAME)



RN 570423-68-6 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[(4-nonylphenyl)methyl]- (9CI) (CA
INDEX NAME)



IT 569685-42-3P 569685-43-4P 569685-49-0P
569685-50-3P

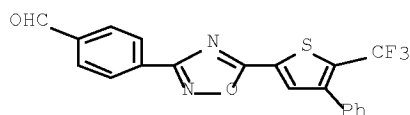
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists
and immunosuppressants: high-throughput screening for oral

10/501176

bioavailability and preparation)

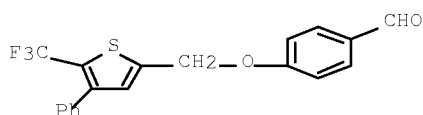
RN 569685-42-3 HCAPLUS

CN Benzaldehyde, 4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



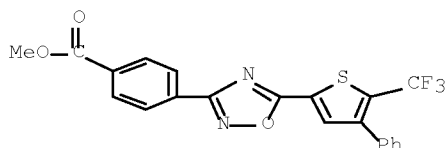
RN 569685-43-4 HCAPLUS

CN Benzaldehyde, 4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]- (9CI) (CA INDEX NAME)



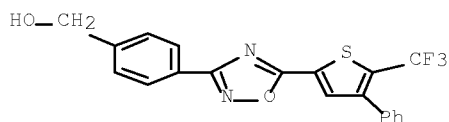
RN 569685-49-0 HCAPLUS

CN Benzoic acid, 4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]-, methyl ester (9CI) (CA INDEX NAME)



RN 569685-50-3 HCAPLUS

CN Benzenemethanol, 4-[5-[4-phenyl-5-(trifluoromethyl)-2-thienyl]-1,2,4-oxadiazol-3-yl]- (CA INDEX NAME)



CC 1-3 (Pharmacology)

Section cross-reference(s): 27

IT 570423-67-5P 570423-76-6P 570423-80-2P
570423-81-3P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral

bioavailability and preparation)
 IT 570423-45-9P 570423-78-8P 828269-16-5P
 828269-17-6P 828269-18-7P 828269-19-8P 828269-20-1P
 828269-21-2P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists
 and immunosuppressants: high-throughput screening for oral
 bioavailability and preparation)
 IT 162359-56-0, FTY 720 256414-75-2 256414-76-3 256414-81-0
 402615-91-2 569683-55-2 570423-38-0
 570423-46-0 570423-68-6 725724-60-7
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists
 and immunosuppressants: high-throughput screening for oral
 bioavailability and preparation)
 IT 146936-34-7P 167279-18-7P 208108-76-3P 256488-46-7P
 569685-42-3P 569685-43-4P 569685-49-0P
 569685-50-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists
 and immunosuppressants: high-throughput screening for oral
 bioavailability and preparation)
 REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT

L134 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:729837 HCAPLUS Full-text

DOCUMENT NUMBER: 141:395611

TITLE: Design and synthesis of conformationally
 constrained 3-(N-alkylamino)propylphosphonic
 acids as potent agonists of
 sphingosine-1-phosphate (S1P) receptors

AUTHOR(S): Yan, Lin; Hale, Jeffrey J.; Lynch, Christopher
 L.; Budhu, Richard; Gentry, Amy; Mills, Sander
 G.; Hajdu, Richard; Keohane, Carol Ann;
 Rosenbach, Mark J.; Milligan, James A.; Shei,
 Gan-Ju; Chrebet, Gary; Bergstrom, James; Card,
 Deborah; Rosen, Hugh; Mandala, Suzanne M.

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck
 Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters
 (2004), 14(19), 4861-4866

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:395611

ED Entered STN: 08 Sep 2004

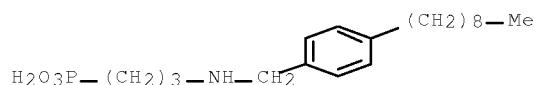
AB Conformationally constrained 3-(N-alkylamino)propylphosphonic acids were systematically
 synthesized and their activities as S1P receptor agonists were evaluated. Several
 pyrrolidine and cyclohexane analogs had S1P receptor profiles comparable to the acyclic
 lead compound, 3-(N-tetradecylamino)propylphosphonic acid (3), lowered circulating
 lymphocytes in mice after iv administration and were thus identified as being suitable
 for further studies.

IT 569684-50-0

RL: PAC (Pharmacological activity); BIOL (Biological study)
 (design and synthesis of conformationally constrained
 (alkylamino)propylphosphonic acids as potent agonists of
 sphingosinephosphate (S1P) receptors)

RN 569684-50-0 HCAPLUS

CN Phosphonic acid, [3-[[[4-nonylphenyl)methyl]amino]propyl]- (9CI)
 (CA INDEX NAME)

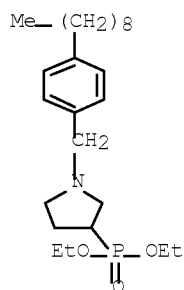


IT 570423-96-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (design and synthesis of conformationally constrained (alkylamino)propylphosphonic acids as potent agonists of sphingosinephosphate (S1P) receptors)

RN 570423-96-0 HCAPLUS

CN Phosphonic acid, [1-[(4-nonylphenyl)methyl]-3-pyrrolidinyl]-, diethyl ester (9CI) (CA INDEX NAME)

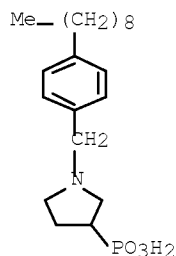


IT 570423-38-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation of alkylpyrrolidinylphosphonate as conformationally constrained (alkylamino)propylphosphonic acids useful as potent agonists of sphingosinephosphate (S1P) receptors)

RN 570423-38-0 HCAPLUS

CN Phosphonic acid, [1-[(4-nonylphenyl)methyl]-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)



CC 29-7 (Organometallic and Organometalloidal Compounds)

Section cross-reference(s): 1

IT 402615-91-2 569684-50-0 725724-60-7 785815-68-1

RL: PAC (Pharmacological activity); BIOL (Biological study)
 (design and synthesis of conformationally constrained (alkylamino)propylphosphonic acids as potent agonists of

sphingosinephosphate (S1P) receptors)

IT 17012-21-4P 157634-00-9P 570423-92-6P ~~570423-96-0P~~
 849811-77-4P 849811-93-4P 849811-94-5P 849812-00-6P
 849812-20-0P 849812-22-2P 849812-30-2P 849812-61-9P
 849813-76-9P 849813-78-1P 849813-85-0P 849813-86-1P
 849813-88-3P 849814-14-8P 849814-16-0P 849814-18-2P
 849814-20-6P 849814-22-8P 849814-23-9P 849815-30-1P
 849816-37-1P 849816-38-2P 849816-39-3P 849816-43-9P
 849816-44-0P 849816-48-4P 849816-51-9P 849816-84-8P
 849817-15-8P 849817-72-7P 849818-04-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (design and synthesis of conformationally constrained
 (alkylamino)propylphosphonic acids as potent agonists of
 sphingosinephosphate (S1P) receptors)

IT 570423-38-0P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 BIOL (Biological study); PREP (Preparation)
 (preparation of alkylpyrrolidinylphosphonate as conformationally
 constrained (alkylamino)propylphosphonic acids useful as potent
 agonists of sphingosinephosphate (S1P) receptors)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT

L134 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:465500 HCAPLUS Full-text

DOCUMENT NUMBER: 141:116457

TITLE: Selecting against S1P3 enhances the acute
 cardiovascular tolerability of
 3-(N-benzyl)aminopropylphosphonic acid S1P
 receptor agonists

AUTHOR(S): Hale, Jeffrey J.; Doherty, George; Toth,
 Leslie; Mills, Sander G.; Hajdu, Richard;
 Keohane, Carol Ann; Rosenbach, Mark; Milligan,
 James; Shei, Gan-Ju; Chrebet, Gary; Bergstrom,
 James; Card, Deborah; Forrest, Michael; Sun,
 Shu-Yu; West, Sarah; Xie, Huijuan; Nomura,
 Naomi; Rosen, Hugh; Mandala, Suzanne

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck
 Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters
 (2004), 14(13), 3501-3505

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:116457

ED Entered STN: 10 Jun 2004

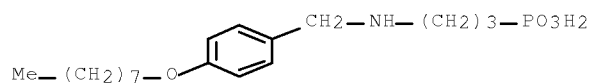
AB Structurally modified 3-(N-benzylamino)propylphosphonic acid S1P receptor agonists that
 maintain affinity for S1P1, and have decreased affinity for S1P3 are efficacious, but
 exhibit decreased acute cardiovascular toxicity in rodents compared to nonselective
 agonists.

IT 569682-67-3P 569682-68-4P 569682-73-1P
 569682-91-3P 569682-93-5P 569682-97-9P
 569682-99-1P 569683-01-8P 569683-30-3P
 569683-32-5P 569683-34-7P 569683-55-2P
 569683-59-6P 569683-61-0P 569683-63-2P
 569683-70-1P 569683-76-7P 569683-78-9P
 569683-81-4P 569683-82-5P 569683-89-2P
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 569684-32-8P 569684-50-0P

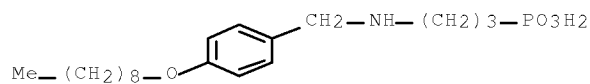
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
 activity); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (selecting against S1P3 enhances acute cardiovascular
 tolerability of 3-(N-benzyl)aminopropylphosphonic acid S1P

receptor agonists)

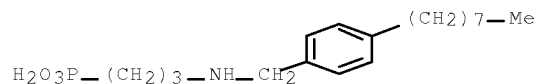
RN 569682-67-3 HCAPLUS

CN Phosphonic acid, [3-[[[4-(octyloxy)phenyl]methyl]amino]propyl]-
(9CI) (CA INDEX NAME)

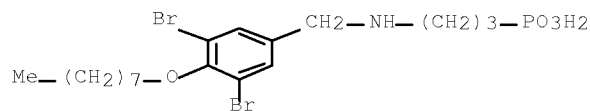
RN 569682-68-4 HCAPLUS

CN Phosphonic acid, [3-[[[4-(nonyloxy)phenyl]methyl]amino]propyl]-
(9CI) (CA INDEX NAME)

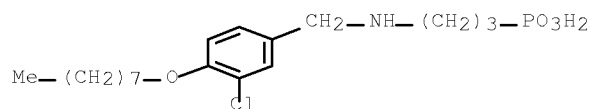
RN 569682-73-1 HCAPLUS

CN Phosphonic acid, [3-[[[4-(octylphenyl)methyl]amino]propyl]- (9CI)
(CA INDEX NAME)

RN 569682-91-3 HCAPLUS

CN Phosphonic acid, [3-[[[3,5-dibromo-4-(octyloxy)phenyl]methyl]amino]
propyl]- (9CI) (CA INDEX NAME)

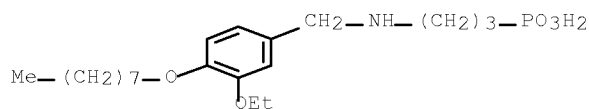
RN 569682-93-5 HCAPLUS

CN Phosphonic acid, [3-[[[3-chloro-4-(octyloxy)phenyl]methyl]amino]pr
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RN 569682-97-9 HCAPLUS

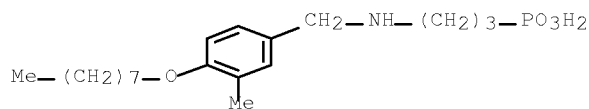
10/501176

CN Phosphonic acid, [3-[[[3-ethoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



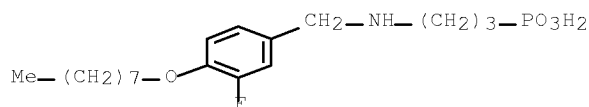
RN 569682-99-1 HCAPLUS

CN Phosphonic acid, [3-[[[3-methyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



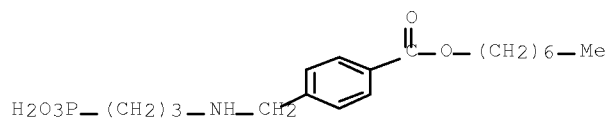
RN 569683-01-8 HCAPLUS

CN Phosphonic acid, [3-[[[3-fluoro-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



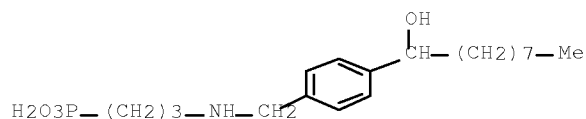
RN 569683-30-3 HCAPLUS

CN Benzoic acid, 4-[[[3-(phosphonopropyl)amino]methyl]-, 1-heptyl ester (9CI) (CA INDEX NAME)



RN 569683-32-5 HCAPLUS

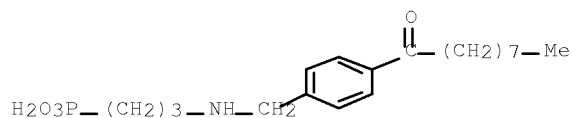
CN Phosphonic acid, [3-[[[4-(1-hydroxynonyl)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



10/501176

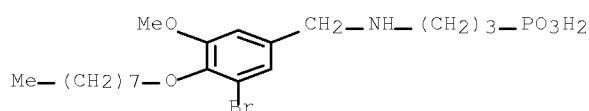
RN 569683-34-7 HCAPLUS

CN Phosphonic acid, [3-[[[4-(1-oxononyl)phenyl]methyl]amino]propyl]-
(9CI) (CA INDEX NAME)



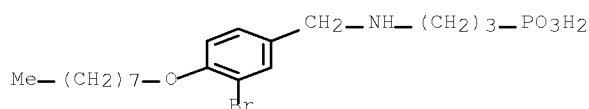
RN 569683-55-2 HCAPLUS

CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



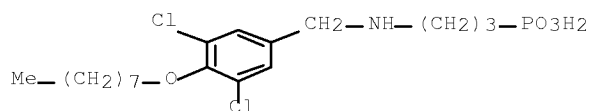
RN 569683-59-6 HCAPLUS

CN Phosphonic acid, [3-[[[3-bromo-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



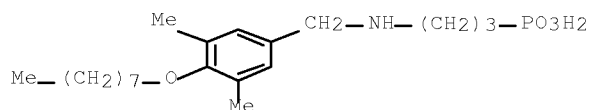
RN 569683-61-0 HCAPLUS

CN Phosphonic acid, [3-[[[3,5-dichloro-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-63-2 HCAPLUS

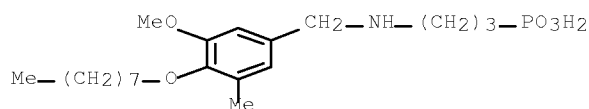
CN Phosphonic acid, [3-[[[3,5-dimethyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



10/501176

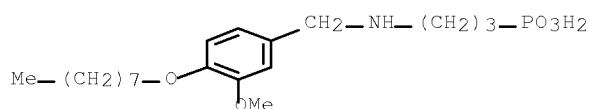
RN 569683-70-1 HCAPLUS

CN Phosphonic acid, [3-[[[3-methoxy-5-methyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



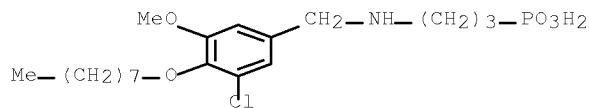
RN 569683-76-7 HCAPLUS

CN Phosphonic acid, [3-[[[3-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



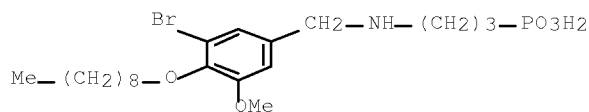
RN 569683-78-9 HCAPLUS

CN Phosphonic acid, [3-[[[3-chloro-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



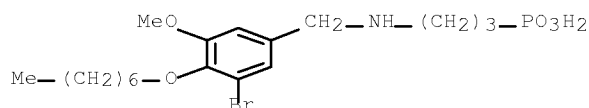
RN 569683-81-4 HCAPLUS

CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(nonyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)

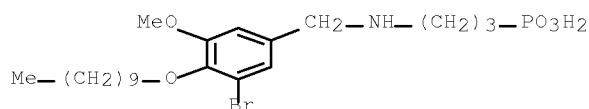


RN 569683-82-5 HCAPLUS

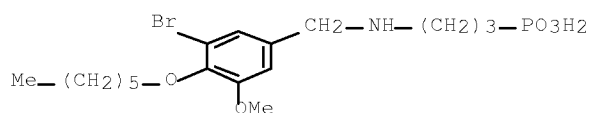
CN Phosphonic acid, [3-[[[3-bromo-4-(heptyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



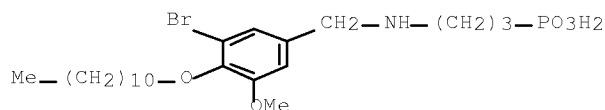
RN 569683-89-2 HCAPLUS
 CN Phosphonic acid, [3-[[[3-bromo-4-(decyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



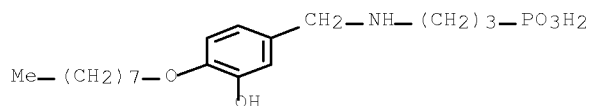
RN 569683-90-5 HCAPLUS
 CN Phosphonic acid, [3-[[[3-bromo-4-(hexyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



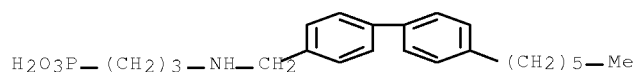
RN 569683-92-7 HCAPLUS
 CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(undecyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



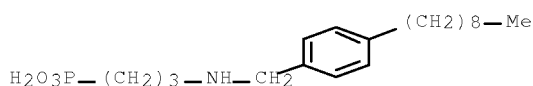
RN 569684-01-1 HCAPLUS
 CN Phosphonic acid, [3-[[[3-hydroxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569684-32-8 HCAPLUS
 CN Phosphonic acid, [3-[[[4'-hexyl[1,1'-biphenyl]-4-yl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569684-50-0 HCAPLUS
 CN Phosphonic acid, [3-[[[4-nonylphenyl)methyl]amino]propyl]- (9CI)
 (CA INDEX NAME)



CC 1-3 (Pharmacology)
 Section cross-reference(s): 25
 IT 569682-67-3P 569682-68-4P 569682-73-1P
 569682-91-3P 569682-93-5P 569682-97-9P
 569682-99-1P 569683-01-8P 569683-30-3P
 569683-32-5P 569683-34-7P 569683-55-2P
 569683-59-6P 569683-61-0P 569683-63-2P
 569683-70-1P 569683-76-7P 569683-78-9P
 569683-81-4P 569683-82-5P 569683-89-2P
 569683-90-5P 569683-92-7P 569684-01-1P
 569684-32-8P 569684-50-0P 724458-96-2P
 724458-97-3P
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (selecting against S1P3 enhances acute cardiovascular tolerability of 3-(N-benzyl)aminopropylphosphonic acid S1P receptor agonists)
 REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT

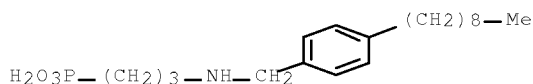
L134 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:465499 HCAPLUS [Full-text](#)
 DOCUMENT NUMBER: 141:133550
 TITLE: The discovery of 3-(N-alkyl)aminopropylphosphonic acids as potent S1P receptor agonists
 AUTHOR(S): Hale, Jeffrey J.; Doherty, George; Toth, Leslie; Li, Zhen; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark; Milligan, James; Shei, Gan-Ju; Chrebet, Gary; Bergstrom, James; Card, Deborah; Rosen, Hugh; Mandala, Suzanne
 CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(13), 3495-3499
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 141:133550
 ED Entered STN: 10 Jun 2004
 AB 3-(N-Alkyl)aminopropylphosphonic acids are potent agonists of four of the five known sphingosine-1-phosphate (S1P) receptor subtypes and are useful in immunosuppressive therapy.
 IT 569684-50-0P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation, immunomodulatory effect and structure-activity

10/501176

relationship studies of 3-(N-alkyl)aminopropylphosphonic acids
as potent S1P receptor agonists)

RN 569684-50-0 HCAPLUS

CN Phosphonic acid, [3-[[4-(nonylphenyl)methyl]amino]propyl]- (9CI)
(CA INDEX NAME)

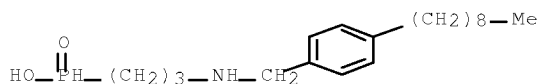


IT 569684-52-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(preparation, immunomodulatory effect and structure-activity
relationship studies of 3-(N-alkyl)aminopropylphosphonic acids
as potent S1P receptor agonists)

RN 569684-52-2 HCAPLUS

CN Phosphonic acid, [3-[[4-(nonylphenyl)methyl]amino]propyl]- (9CI)
(CA INDEX NAME)



CC 1-3 (Pharmacology)

Section cross-reference(s): 21

IT 569684-50-0P 725724-58-3P 725724-59-4P 725724-60-7P
725724-61-8P 725724-62-9P 725724-63-0P 725724-64-1P
725724-65-2P 725724-66-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(preparation, immunomodulatory effect and structure-activity
relationship studies of 3-(N-alkyl)aminopropylphosphonic acids
as potent S1P receptor agonists)

IT 402615-91-2 569682-76-4 569682-79-7 569682-80-0
569682-84-4 569682-85-5 569682-86-6 569684-52-2
5696819-84-0 597340-18-6 597340-90-4 597340-97-1
597341-03-2 597341-12-3 725724-57-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(preparation, immunomodulatory effect and structure-activity
relationship studies of 3-(N-alkyl)aminopropylphosphonic acids
as potent S1P receptor agonists)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L134 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:368306 HCAPLUS Full-text

DOCUMENT NUMBER: 141:99302

TITLE: Immune cell regulation and cardiovascular
effects of sphingosine 1-phosphate receptor
agonists in rodents are mediated via distinct
receptor subtypes

AUTHOR(S): Forrest, M.; Sun, S.-Y.; Hajdu, R.; Bergstrom,
J.; Card, D.; Doherty, G.; Hale, J.; Keohane,
C.; Meyers, C.; Milligan, J.; Mills, S.;

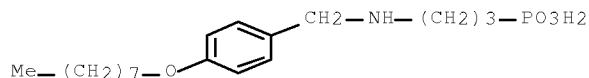
10/501176

Nomura, N.; Rosen, H.; Rosenbach, M.; Shei, G.-J.; Singer, I. I.; Tian, M.; West, S.; White, V.; Xie, J.; Proia, R. L.; Mandala, S.
 CORPORATE SOURCE: Departments of Immunology and Rheumatology, Pharmacology, and Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, USA
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(2), 758-768
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 06 May 2004

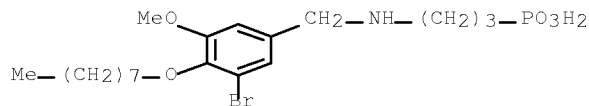
AB Sphingosine 1-phosphate (S1P) is a bioactive lysolipid with pleiotropic functions mediated through a family of G protein-coupled receptors, S1P1,2,3,4,5. Physiol. effects of S1P receptor agonists include regulation of cardiovascular function and immunosuppression via redistribution of lymphocytes from blood to secondary lymphoid organs. The phosphorylated metabolite of the immunosuppressant agent FTY720 (2-amino-2-(2-[4-octylphenyl]ethyl)-1,3-propanediol) and other phosphonate analogs with differential receptor selectivity were investigated. No significant species differences in compound potency or rank order of activity on receptors cloned from human, murine, and rat sources were observed. All synthetic analogs were high-affinity agonists on S1P1, with IC50 values for ligand binding between 0.3 and 14 nM. The correlation between S1P1 receptor activation and the ED50 for lymphocyte reduction was highly significant ($p < 0.001$) and lower for the other receptors. In contrast to S1P1-mediated effects on lymphocyte recirculation, three lines of evidence link S1P3 receptor activity with acute toxicity and cardiovascular regulation: compound potency on S1P3 correlated with toxicity and bradycardia; the shift in potency of phosphorylated-FTY720 for inducing lymphopenia vs. bradycardia and hypertension was consistent with affinity for S1P1 relative to S1P3; and toxicity, bradycardia, and hypertension were absent in S1P3-/- mice. Blood pressure effects of agonists in anesthetized rats were complex, whereas hypertension was the predominant effect in conscious rats and mice. Immunolocalization of S1P3 in rodent heart revealed abundant expression on myocytes and perivascular smooth muscle cells consistent with regulation of bradycardia and hypertension, whereas S1P1 expression was restricted to the vascular endothelium.

IT 569682-67-3 569683-55-2 569683-90-5
 RL: PAC (Pharmacological activity); BIOL (Biological study)
 (immune cell regulation and cardiovascular effects of sphingosine 1-phosphate receptor agonists in rodents are mediated via distinct receptor subtypes)

RN 569682-67-3 HCAPLUS
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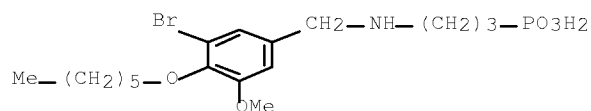


RN 569683-55-2 HCAPLUS
 CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



10/501176

RN 569683-90-5 HCAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(hexyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



CC 1-7 (Pharmacology)
IT 26993-30-6, Sphingosine 1 phosphate 402615-91-2
569682-67-3 569683-55-2 569683-90-5
719286-66-5 719286-67-6
RL: PAC (Pharmacological activity); BIOL (Biological study)
(immune cell regulation and cardiovascular effects of
sphingosine 1-phosphate receptor agonists in rodents are
mediated via distinct receptor subtypes)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

FULL SEARCH HISTORY

=> d his nofile

(FILE 'HOME' ENTERED AT 09:32:45 ON 27 JUL 2007)

FILE 'HCAPLUS' ENTERED AT 09:33:39 ON 27 JUL 2007

E US20050070506/PN

L1 1 SEA ABB=ON PLU=ON US20050070506/PN
 D ALL
 SEL RN

FILE 'REGISTRY' ENTERED AT 09:34:34 ON 27 JUL 2007

L2 424 SEA ABB=ON PLU=ON (100-83-4/BI OR 101385-93-7/BI OR
 101500-22-5/BI OR 103057-44-9/BI OR 103680-62-2/BI OR
 103680-71-3/BI OR 10521-91-2/BI OR 106-41-2/BI OR
 107-13-1/BI OR 108898-23-3/BI OR 110943-74-3/BI OR
 111-70-6/BI OR 111-86-4/BI OR 1203-68-5/BI OR 1204-60-0
 /BI OR 121-32-4/BI OR 121-33-5/BI OR 121118-78-3/BI OR
 123-08-0/BI OR 130592-02-8/BI OR 13138-33-5/BI OR
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 569682-78-6/BI OR 569682-79-7/BI OR 569682-80-0/BI OR
 569682-81-1/BI OR 569

L3 71 SEA ABB=ON PLU=ON L2 AND 1/NR AND 1/P AND 1/N
 D 1-3 STR RSD

L4 154 SEA ABB=ON PLU=ON L2 AND 1/P

FILE 'HCAPLUS' ENTERED AT 09:39:18 ON 27 JUL 2007

L5 140355 SEA ABB=ON PLU=ON L2

FILE 'REGISTRY' ENTERED AT 09:39:32 ON 27 JUL 2007

FILE 'HCAPLUS' ENTERED AT 09:42:04 ON 27 JUL 2007

D SCAN L1

FILE 'REGISTRY' ENTERED AT 09:42:05 ON 27 JUL 2007

L6 23 SEA ABB=ON PLU=ON L4 AND C4N/RF
 D SCAN

L7 0 SEA ABB=ON PLU=ON L6 AND C4S/RF

L8 36 SEA ABB=ON PLU=ON L2 AND C4S/RF

10/501176

D SCAN
L9 67 SEA ABB=ON PLU=ON L2 AND C4N/RF
L10 7 SEA ABB=ON PLU=ON L8 AND L9
D SCAN

FILE 'STNGUIDE' ENTERED AT 09:47:31 ON 27 JUL 2007

FILE 'REGISTRY' ENTERED AT 09:58:25 ON 27 JUL 2007
L11 7 SEA ABB=ON PLU=ON L2 AND C2N2O/RF
L12 1 SEA ABB=ON PLU=ON L10 AND L11
D SCAN
D SCAN L12
D SCAN L11
L13 43 SEA ABB=ON PLU=ON L2 AND 3/F
L14 36 SEA ABB=ON PLU=ON L13 AND L8
L15 7 SEA ABB=ON PLU=ON L13 AND L10
D SCAN

FILE 'STNGUIDE' ENTERED AT 10:03:40 ON 27 JUL 2007

FILE 'REGISTRY' ENTERED AT 10:05:33 ON 27 JUL 2007
L16 12 SEA ABB=ON PLU=ON L2 AND C3N/RF
D SCAN

FILE 'STNGUIDE' ENTERED AT 10:06:39 ON 27 JUL 2007

FILE 'REGISTRY' ENTERED AT 10:07:56 ON 27 JUL 2007
L17 6 SEA ABB=ON PLU=ON L16 AND L8
L18 1 SEA ABB=ON PLU=ON L16 AND L11

FILE 'STNGUIDE' ENTERED AT 10:08:37 ON 27 JUL 2007
D SCAN L18

FILE 'REGISTRY' ENTERED AT 10:08:53 ON 27 JUL 2007
D SCAN L17
D SCAN L18

FILE 'STNGUIDE' ENTERED AT 10:09:12 ON 27 JUL 2007

FILE 'REGISTRY' ENTERED AT 10:12:52 ON 27 JUL 2007
D RSD
L19 40 SEA ABB=ON PLU=ON L9 AND C6/RF AND 2/NR
L20 9 SEA ABB=ON PLU=ON L19 AND 4/O
D SCAN
L21 1 SEA ABB=ON PLU=ON L20 AND C22 H33 N O4/MF
L22 2 SEA ABB=ON PLU=ON L9 AND 1/F
D SCAN
D SCAN L12
L23 1 SEA ABB=ON PLU=ON L16 AND 2/NR AND 2/O
D SCAN
L24 22 SEA ABB=ON PLU=ON L9 AND 2/NR AND 2-3/O AND C6/RF
L25 11 SEA ABB=ON PLU=ON L24 AND 2/O
D SCAN
L26 2 SEA ABB=ON PLU=ON L25 AND 21/C
D SCAN
L27 4 SEA ABB=ON PLU=ON L24 AND 20/C AND 3/O
D SCAN
L28 6 SEA ABB=ON PLU=ON L2 AND 2/BR
D SCAN
L29 3 SEA ABB=ON PLU=ON L28 AND 2/NR
D SCAN
D QUE
L30 6 SEA ABB=ON PLU=ON L9 AND 2/NR AND 5/O AND 1/P
D SCAN
L31 6 SEA ABB=ON PLU=ON L15 AND 4/NR
L32 5 SEA ABB=ON PLU=ON L31 AND 3/O
D SCAN

10/501176

L33 27 SEA ABB=ON PLU=ON L3 AND 4/O
L34 10 SEA ABB=ON PLU=ON L2 AND ?NAPHTH?/CNS
D SCAN
L35 5 SEA ABB=ON PLU=ON L34 AND 20-30/C
D SCAN
L36 92 SEA ABB=ON PLU=ON L2 AND 2/NR NOT ((L8 OR L9) OR 11)
L37 44 SEA ABB=ON PLU=ON L2 AND ?BIPHENYL?/CNS
D SCAN

FILE 'STNGUIDE' ENTERED AT 10:53:32 ON 27 JUL 2007

FILE 'REGISTRY' ENTERED AT 10:57:53 ON 27 JUL 2007

L38 32 SEA ABB=ON PLU=ON L37 AND 20-100/C
L39 0 SEA ABB=ON PLU=ON L38 AND 1/S
D QUE
L40 0 SEA ABB=ON PLU=ON L37 AND 1-5/S
D SCAN L3
L41 68 SEA ABB=ON PLU=ON L3 AND C6/RF
L42 68 SEA ABB=ON PLU=ON L41 AND 12-50/C
D SCAN

FILE 'STNGUIDE' ENTERED AT 11:12:32 ON 27 JUL 2007

FILE 'REGISTRY' ENTERED AT 11:18:09 ON 27 JUL 2007

L43 157 SEA ABB=ON PLU=ON L6 OR (L10 OR L11 OR L12 OR L13 OR
L14 OR L15 OR L16 OR L17 OR L18) OR (L19 OR L20 OR L21
OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR
L29 OR L30 OR L31 OR L32 OR L33) OR L35 OR L38
L44 199 SEA ABB=ON PLU=ON (L41 OR L42 OR L43)

FILE 'HCAPLUS' ENTERED AT 11:20:11 ON 27 JUL 2007

L45 849 SEA ABB=ON PLU=ON L44
L46 QUE ABB=ON PLU=ON PHARMAC?/SC,SX
L47 483 SEA ABB=ON PLU=ON L45 AND L46
D SCAN L1
L48 QUE ABB=ON PLU=ON PY<2003 OR PRY<2003 OR AY<2003 OR
MY<2003 OR REVIEW/DT
L49 270 SEA ABB=ON PLU=ON L47 AND L48
L50 QUE ABB=ON PLU=ON IMMUNOSUPPRES? OR IMMUNOREG? OR
IMMUN?(A) (SUPPRESS? OR REG?)
L51 7 SEA ABB=ON PLU=ON L49 AND L50
D SCAN
E IMMUNOSUPPRESSIVES/CT
E IMMUNOSUP/CT
L52 QUE ABB=ON PLU=ON IMMUNOSUPPRESSANTS+PFT, OLD, NT/CT
L53 QUE ABB=ON PLU=ON IMMUNOSUPPRESSION+PFT, OLD, NT/CT
E AGONIS/CT
E AGON/CT
L54 6 SEA ABB=ON PLU=ON L49 AND (L52 OR L53)
D SCAN
E ANTAGONISTS/CT
E ANTAG/CT
E ANTAGONISM/CT
E E3+ALL
L55 QUE ABB=ON PLU=ON ANTAGONISM+PFT, OLD, NT/CT
L56 0 SEA ABB=ON PLU=ON L49 AND L55
L57 QUE ABB=ON PLU=ON AGON? OR ANTAG?
L58 79 SEA ABB=ON PLU=ON L49 AND L57
D L***-L*** KWIC
D 70-79 KWIC
L59 QUE ABB=ON PLU=ON EDG1(A)S1P?
L60 19 SEA ABB=ON PLU=ON EDG1(A)S1P?
D 1-3 KWIC
L61 2 SEA ABB=ON PLU=ON L60 AND L49
D 1-2 KWIC
L62 QUE ABB=ON PLU=ON F(W)Y

L63 0 SEA ABB=ON PLU=ON L49 AND L62
 E EDG1 RECEPTOR/CT
 E EDG1 AGONIST/CT
 E FTY/CT
 E GTP/CT
 E E3+ALL
 E GTP/CT
 L64 QUE ABB=ON PLU=ON GTP? OR FTP?
 L65 0 SEA ABB=ON PLU=ON L49 AND L64
 L66 QUE ABB=ON PLU=ON 720
 L67 0 SEA ABB=ON PLU=ON L49 AND L66
 L68 QUE ABB=ON PLU=ON AUTOIMMUN?
 L69 21 SEA ABB=ON PLU=ON L49 AND L68
 D 1-5 KWIC
 L70 QUE ABB=ON PLU=ON "AUTOIMMUNE DISEASE"+PFT, OLD, NT/CT
 L71 32 SEA ABB=ON PLU=ON L49 AND L70
 D SCAN L1
 E INFLAMMATION/CT
 L72 QUE ABB=ON PLU=ON INFLAMMATION+PFT, OLD, NT/CT
 L73 41 SEA ABB=ON PLU=ON L49 AND L72
 E INFECTION/CT
 E INFECTIONS/CT
 L74 QUE ABB=ON PLU=ON INFECTION+PFT, OLD, NT/CT
 L75 15 SEA ABB=ON PLU=ON L49 AND L74
 L76 QUE ABB=ON PLU=ON AIDS+PFT, OLD, NT/CT
 L77 7 SEA ABB=ON PLU=ON L49 AND L76
 L78 QUE ABB=ON PLU=ON ASTHMA+PFT, OLD, NT/CT
 L79 16 SEA ABB=ON PLU=ON L49 AND L78
 D L1 IT
 L80 QUE ABB=ON PLU=ON "RESPIRATORY SYSTEM, DISEASE"+PFT, O
 LD, NT/CT
 L81 29 SEA ABB=ON PLU=ON L49 AND L80
 L82 QUE ABB=ON PLU=ON ARTHRITIS+PFT, OLD, NT/CT
 L83 22 SEA ABB=ON PLU=ON L49 AND L82
 E MUSCULAR DYSTRO/CT
 L84 QUE ABB=ON PLU=ON "MUSCULAR DYSTROPHY"+PFT, OLD, NT/CT
 L85 3 SEA ABB=ON PLU=ON L49 AND L84
 L86 QUE ABB=ON PLU=ON "SKIN, DISEASE"+PFT, OLD, NT/CT
 L87 30 SEA ABB=ON PLU=ON L49 AND L86
 E DERMATITIS/CT
 E E3+ALL
 L88 QUE ABB=ON PLU=ON DERMATITIS+PFT, OLD, NT/CT
 L89 12 SEA ABB=ON PLU=ON L49 AND L88
 L90 68 SEA ABB=ON PLU=ON L51 OR L61 OR L69 OR L71 AND L73
 OR L75 OR L77 OR L79 OR L81 OR L83 OR L85 OR L89 OR
 L87
 L91 24 SEA ABB=ON PLU=ON L58 AND L90
 L92 7 SEA ABB=ON PLU=ON L90 AND L50
 L93 2 SEA ABB=ON PLU=ON L90 AND L60
 L94 QUE ABB=ON PLU=ON NEOPLASM+PFT, OLD, NT/CT
 L95 44 SEA ABB=ON PLU=ON L49 AND L94
 L96 32 SEA ABB=ON PLU=ON L95 AND L90
 SAV L96 JEA176HCP/A
 DEL SEL
 SEL L96 HIT RN
 D SCAN
 DEL SEL
 SEL L1 AU
 L97 1272 SEA ABB=ON PLU=ON ("DOHERTY, GEORGE A."/AU OR
 "FORREST, MICHAEL J."/AU OR "HAJDU, RICHARD"/AU OR
 "HALE, JEFFREY J."/AU OR "LI, ZHEN"/AU OR "MANDALA,
 SUZANNE M."/AU OR "MILLS, SANDER G."/AU OR "ROSEN,
 HUGH"/AU OR "SCOLNICK, EDWARD M."/AU)
 L98 QUE ABB=ON PLU=ON MERCK?/PA, CS, SO, CO
 L99 714 SEA ABB=ON PLU=ON L97 AND L48

10/501176

L100 228 SEA ABB=ON PLU=ON L99 AND L98
L101 26 SEA ABB=ON PLU=ON L100 AND L50
L102 1 SEA ABB=ON PLU=ON L1 AND L101
L103 28 SEA ABB=ON PLU=ON L96 NOT L101
D SCAN

FILE 'REGISTRY' ENTERED AT 12:08:47 ON 27 JUL 2007

L104 1 SEA ABB=ON PLU=ON 3300-51-4/RN
D SCAN

FILE 'STNGUIDE' ENTERED AT 12:10:46 ON 27 JUL 2007

FILE 'REGISTRY' ENTERED AT 12:12:43 ON 27 JUL 2007

L105 179 SEA ABB=ON PLU=ON L44 AND 18-70/C

FILE 'HCAPLUS' ENTERED AT 12:13:38 ON 27 JUL 2007

L106 15 SEA ABB=ON PLU=ON L105
L107 0 SEA ABB=ON PLU=ON L106 AND L103
D SCAN L106
D L106 1-15 CC
L108 3 SEA ABB=ON PLU=ON L106 AND L48
D SCAN

FILE 'REGISTRY' ENTERED AT 12:18:30 ON 27 JUL 2007

L109 20 SEA ABB=ON PLU=ON L44 NOT L105
D SCAN
L110 1 SEA ABB=ON PLU=ON L109 AND C14 H24 N O4 P/MF
L111 1 SEA ABB=ON PLU=ON L109 AND C17 H29 BR N O5 P/MF
L112 181 SEA ABB=ON PLU=ON L105 OR L110 OR L111

FILE 'HCAPLUS' ENTERED AT 12:23:02 ON 27 JUL 2007

L113 15 SEA ABB=ON PLU=ON L112
L114 15 SEA ABB=ON PLU=ON L106 OR L113
L115 3 SEA ABB=ON PLU=ON L114 AND L48
L116 3 SEA ABB=ON PLU=ON L115 AND (L50 OR (L52 OR L53) OR
L55 OR L57 OR L59 OR L70 OR L72 OR L74 OR L76 OR L78
OR L80)
L117 3 SEA ABB=ON PLU=ON L116 AND (L82 OR L84 OR L86 OR L88
OR L94)
D SCAN
SAV L117 JEA176HCPA/A
L118 3 SEA ABB=ON PLU=ON L117 NOT L103
L119 0 SEA ABB=ON PLU=ON L117 NOT L101
L120 4 SEA ABB=ON PLU=ON L96 AND L50
D SCAN
L121 0 SEA ABB=ON PLU=ON L120 NOT L101
D QUE L101
L122 12 SEA ABB=ON PLU=ON L113 NOT (L118 OR L120)
D SCAN
SAV L122 JEA176HCPB/A

FILE 'REGISTRY' ENTERED AT 12:39:55 ON 27 JUL 2007

L123 0 SEA ABB=ON PLU=ON L112 AND MEDLINE/LC
L124 0 SEA ABB=ON PLU=ON L112 AND BIOSIS/LC
L125 0 SEA ABB=ON PLU=ON L112 AND DRUGU/LC
L126 0 SEA ABB=ON PLU=ON L112 AND EMBASE/LC
D QUE

FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 12:40:59 ON 27
JUL 2007

L127 0 SEA ABB=ON PLU=ON L126
L128 608 SEA ABB=ON PLU=ON L97
L129 277 SEA ABB=ON PLU=ON L128 AND L98
L130 143 SEA ABB=ON PLU=ON L129 AND L48
L131 6 SEA ABB=ON PLU=ON L130 AND (L50 OR L59)
D 1-6 TI
SAV L131 JEA176MULTIN/A

10/501176

FILE 'STNGUIDE' ENTERED AT 12:44:10 ON 27 JUL 2007

FILE 'HCAPLUS' ENTERED AT 12:45:23 ON 27 JUL 2007
SAV L101 JEA176HCPIN/A

FILE 'STNGUIDE' ENTERED AT 12:46:17 ON 27 JUL 2007
D QUE L101
D QUE L101
D QUE L131

FILE 'HCAPLUS, MEDLINE, BIOSIS' ENTERED AT 12:49:36 ON 27 JUL 2007
L132 29 DUP REM L101 L131 (3 DUPLICATES REMOVED)
ANSWERS '1-26' FROM FILE HCAPLUS
ANSWERS '27-29' FROM FILE BIOSIS
D L132 1-29 IBIB ED AB
L133 4 SEA ABB=ON PLU=ON (L106 OR L96) AND L101
D SCAN
D QUE L133
D L133 1-4 IBIB ED ABS FHITSTR HITIND

FILE 'STNGUIDE' ENTERED AT 13:04:20 ON 27 JUL 2007
D QUE L119
D QUE L121
D QUE L122
D QUE L127

FILE 'HCAPLUS' ENTERED AT 13:06:51 ON 27 JUL 2007
L134 12 DUP REM L119 L121 L122 L127 (0 DUPLICATES REMOVED)
ANSWERS '1-12' FROM FILE HCAPLUS
D L134 1-12 IBIB ED ABS HITSTR HITIND